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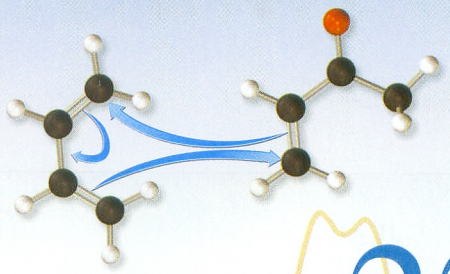

Pericyclic Reactions

CHAPTER 22

Most of the reactions presented in previous chapters involved nucleophiles and electrophiles and occurred in several steps involving cationic, anionic, or, in the last chapter, radical intermediates. In this chapter a group of concerted (one-step) reactions, called pericyclic reactions, that involve none of these intermediates is discussed. The mechanisms of these reactions are exceedingly simple because they consist of a single step. Yet, as we shall see, pericyclic reactions are amazingly selective, both in terms of when they occur and also in their stereochemical requirements.

First, pericyclic reactions are defined, and an example of their unusual stereochemical selectivity is presented. A theoretical treatment of pericyclic reactions requires examination of the MOs for the conjugated molecules that participate in these reactions, so MO theory for these compounds is developed next. Then a theoretical explanation for the selectivity and stereochemistry observed in each of the three classes of pericyclic reactions is presented, along with a number of common examples of reactions of each kind.

22.1 Pericyclic Reactions

A **pericyclic reaction** is concerted and proceeds through a cyclic transition state in which two or more bonds are made and/or broken. As a concerted reaction, it does not involve any detectable ionic or radical intermediates. The effect of changing the polarity of the solvent is usually small, indicating the lack of significant charge buildup in the transition state. These reactions are highly stereospecific, and the stereochemistry often changes when the energy for the reaction is supplied by heat (**thermolysis** or **pyrolysis**) as compared to when it is supplied by light (**photolysis**).

Mastering Organic Chemistry

- Understanding the Energies and Nodal Properties of the Pi MOs of a Conjugated System
- Recognizing Electrocyclic Reactions, Cycloaddition Reactions, and Sigmatropic Rearrangements
- Using Pi MOs to Determine Whether These Reactions Are Allowed or Forbidden
- Predicting the Products, Including Stereochemistry, of These Reactions
- Understanding the Mechanisms of the Pinacol, Beckmann, Hofmann, and Baeyer-Villiger Rearrangements
- Understanding the Mechanism, Selectivity, and Stereochemistry of Pericyclic Reactions
- Using These Reactions in Synthesis

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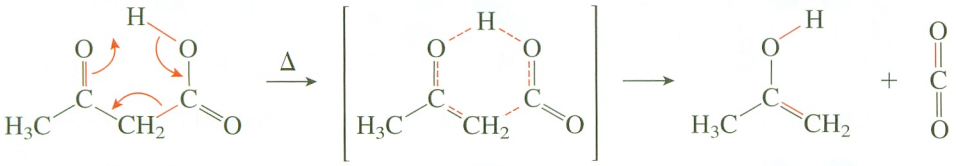
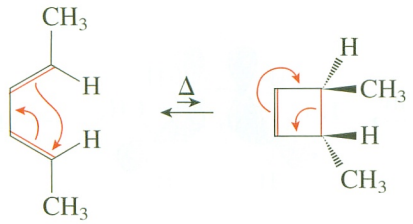
An example of a reaction, first presented in Section 20.4, that falls under the pericyclic classification is the decarboxylation of β-ketoacids produced in the malonic and acetoacetic ester syntheses:



Transition state

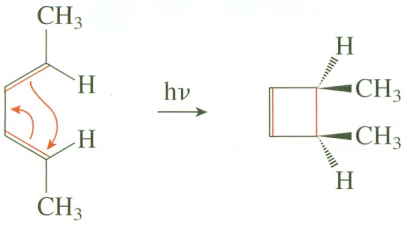
This cyclic movement of electrons and a transition state that involves a cycle of breaking and forming bonds are characteristics of a pericyclic reaction.

An example of a pericyclic reaction that illustrates the rather amazing stereoselectivity that these reactions often exhibit is provided by the thermal and photochemical interconversions of dienes and cyclobutenes. When (2*E*,4*E*)-hexadiene is heated, it cyclizes to form *trans*-3,4-dimethylcyclobutene. None of the *cis*-isomer is produced. In the reverse reaction the cyclobutene opens to produce only the (*E*,*E*)-isomer of the hexadiene. The reaction is completely stereospecific in both directions:



(2*E*,4*E*)-Hexadiene *trans*-3,4-Dimethylcyclobutene

Making the stereochemical results even more remarkable, if the same stereoisomer of the hexadiene is photolyzed, rather than heated, *cis*-3,4-dimethylcyclobutene is the only product formed:

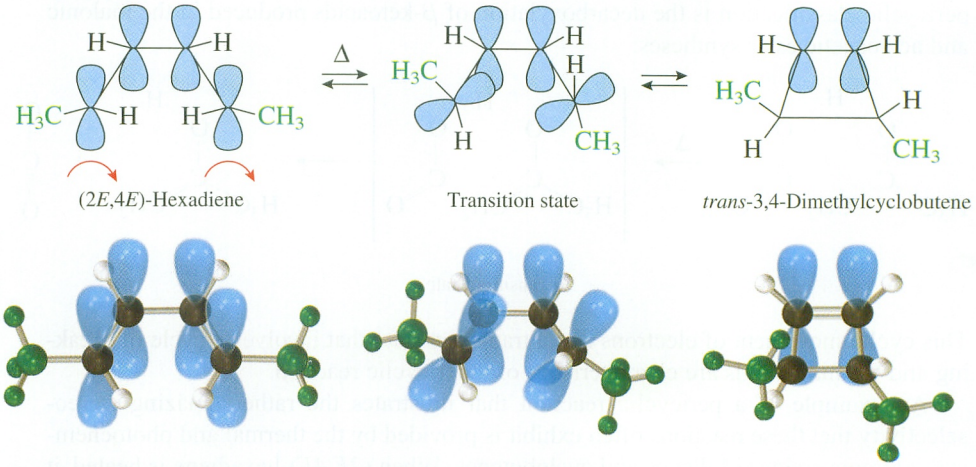


(2*E*,4*E*)-Hexadiene *cis*-3,4-Dimethylcyclobutene

The stereochemistry of the photochemical reaction is the opposite of that of the thermal reaction!

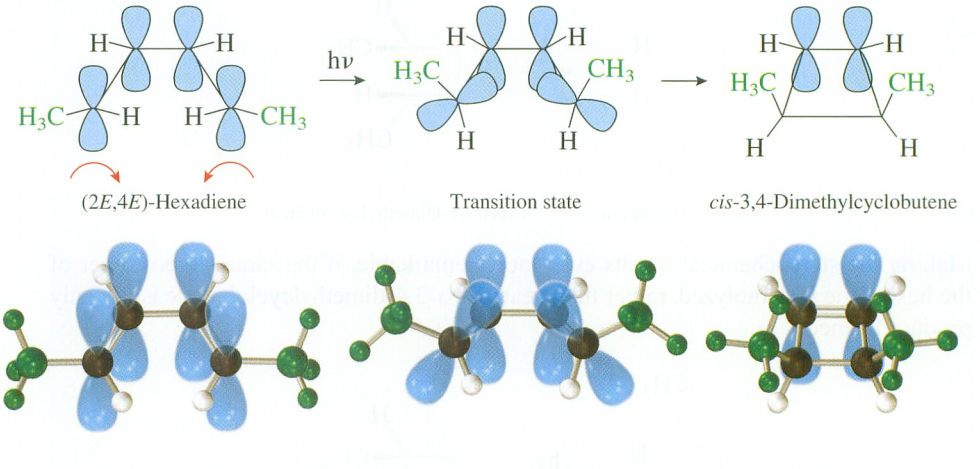
Let's carefully compare the movements of the atoms that must occur in these reactions to cause such different stereochemical results. As shown in Figure 22.1, the process is quite simple. The two end carbons of the conjugated pi system need only rotate so that their *p* orbitals begin to overlap to form the new sigma bond of the cyclobutene. In the case of the thermal reaction, both carbons rotate in the same direction, a process that is

Conrotation



When (2*E*,4*E*)-hexadiene is heated, only *trans*-3,4-dimethylcyclobutene is produced. The end carbons of the conjugated diene system rotate in the same direction (both clockwise or both counterclockwise). This is called **conrotation.**

Disrotation



In the photochemical reaction, the end carbons of the conjugated diene system rotate in opposite directions (one clockwise and one counterclockwise) so that cis-3,4-dimethylcyclobutene is produced. This is called **disrotation.**

Active Figure 22.1

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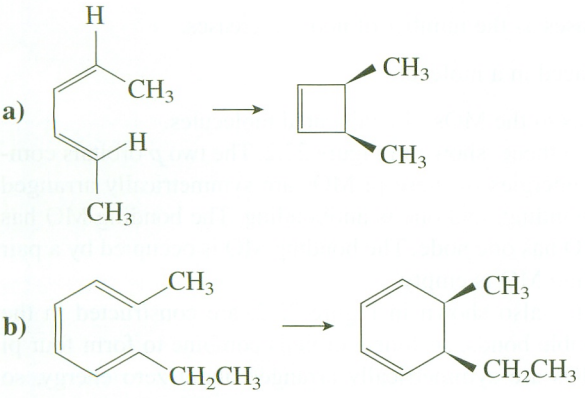
BOND ROTATIONS IN THE REACTIONS OF 2,4-HEXADIENE TO PRODUCE 3,4-DIMETHYLCYCLOBUTENE. Test yourself on the concepts in this figure at **OrganicChemistryNow.**

termed **conrotation,** so the methyl groups have a trans orientation in the cyclobutene product. The hybridization of these carbons changes from sp^2 to sp^3 as the rotation occurs. The two *p* orbitals on the central carbons of the diene system form the new pi bond. The process is very similar for the photochemical reaction, with the exception that the end carbons rotate in opposite directions, a process termed **disrotation,** so that the

methyl groups have a cis orientation in the cyclobutene product. There is no obvious reason why conrotation should be preferred over disrotation in the thermal reaction, much less why this preference is reversed in the photochemical reaction.

PROBLEM 22.1

Determine whether these reactions occur by conrotation or disrotation:



MODEL BUILDING PROBLEM 22.1

You will find a set of handheld models invaluable in helping to visualize the stereochemistry of the reactions in this chapter. Build a model of (2*E*,4*E*)-hexadiene and examine both conrotation to give *trans*-3,4-dimethylcyclobutene and disrotation to give *cis*-3,4-dimethylcyclobutene.

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Click *Molecular Models* to view computer models of the molecules in this chapter.

These apparently simple reactions were poorly understood by organic chemists until 1965, when R. B. Woodward and R. Hoffmann developed a theoretical explanation for the selectivities. A related theory was developed by K. Fukui at about the same time. (Fukui and Hoffmann shared the 1981 Nobel Prize in chemistry for this work. Woodward died in 1979 and so did not share in this award because the Nobel Prize is not given posthumously. However, he had already won a Nobel Prize in 1965 for his work in the area of organic synthesis.)

Both of these theories explain whether the transition state for the reaction under consideration is favorable or not by examining how the reactant MOs are converted to the product MOs. To understand and use these theories, we need to first discuss the MOs for the conjugated molecules that participate in these reactions.

22.2 MO Theory for Conjugated Molecules

A model for localized MOs—that is, MOs that extend over only two atoms—was developed in Chapter 3. To describe conjugated molecules, MOs that extend over more than two atoms, delocalized MOs, are needed. Some aspects of the theory for delocalized MOs were presented in Chapters 15 and 16; all of the important aspects are reiterated here.

To explain pericyclic reactions, the energies and the location of the nodes of the pi MOs of noncyclic, linear, conjugated molecules are needed. These can be obtained by the application of the following rules:

1. The number of MOs equals the number of AOs combining to form them.
2. The energies of the MOs are symmetrically placed about the energy of an isolated *p* orbital (arbitrarily taken as zero energy).
3. The energy of an MO increases as the number of nodes increases.
4. Nodes are symmetrically placed in a molecule.

Let's see how to apply these rules to the MOs of conjugated molecules.

First, consider the pi MOs of ethene, shown in Figure 22.2. The two *p* orbitals combine to form two pi MOs. The energies of these pi MOs are symmetrically arranged about zero energy; one MO is bonding, and one is antibonding. The bonding MO has no node, and the antibonding MO has one node. The bonding MO is occupied by a pair of electrons, while the antibonding MO is empty.

The pi MOs of 1,3-butadiene, also shown in Figure 22.2, are constructed in the same manner. There are two double bonds, so four *p* orbitals combine to form four pi MOs. The energies of these MOs are symmetrically arranged about zero energy, so

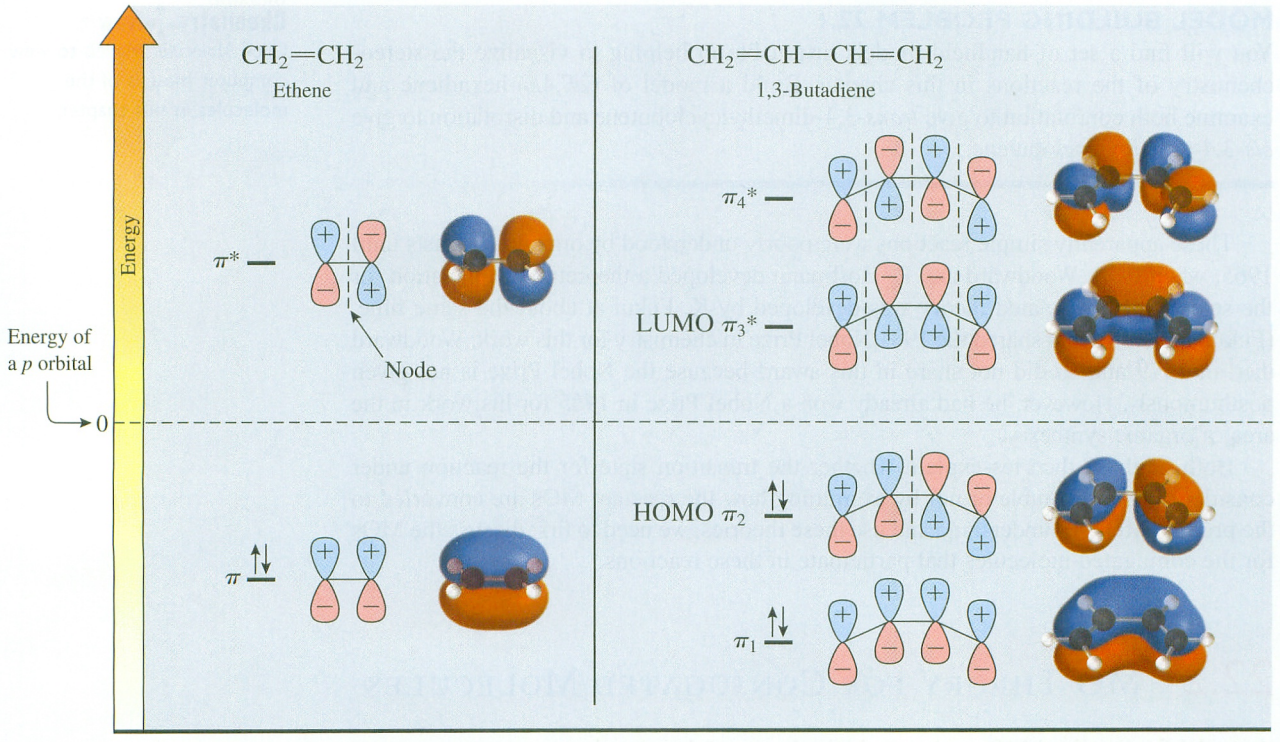


Figure 22 .2

ENERGIES AND NODAL PROPERTIES FOR THE PI MOS OF ETHENE AND 1,3-BUTADIENE.

there are two bonding MOs and two antibonding MOs. The lowest-energy MO, π_1, has zero nodes. All of its AOs overlap in a bonding fashion; that is, a plus lobe of one orbital overlaps with the plus lobe of the adjacent orbital (or a minus lobe overlaps with a minus lobe). The next MO, π_2, has one node, placed symmetrically in the molecule, between the two central carbons. In this MO, two of the overlaps of the *p* AOs are bonding in nature, and one of the overlaps, in the center of the molecule, is antibonding in nature because the plus lobe of one orbital overlaps with the minus lobe of the other. This orbital is overall bonding because it has two favorable (bonding) overlaps and only one unfavorable (antibonding) overlap. The next MO, π_3*, has two nodes that are again symmetrically placed in the molecule. It is a net antibonding MO because two of the overlaps are antibonding in nature, while only one is bonding. Finally, π_4* has three nodes. It is the highest-energy MO because the overlaps of all of the *p* AOs are antibonding in nature. There are four pi electrons, so the two bonding MOs, π_1 and π_2, are both occupied by a pair of electrons. The highest-energy orbital that contains an electron, π_2 in this case, is termed the **highest occupied molecular orbital (HOMO),** and the lowest-energy orbital that contains no electrons, π_3* in this case, is termed the **lowest unoccupied molecular orbital (LUMO).**

Figure 22.3 shows the pi molecular orbitals for the system of six conjugated *p* orbitals, 1,3,5-hexatriene. The six *p* AOs combine to form six pi MOs. These are arranged symmetrically about zero energy, so there are three bonding MOs and three antibonding MOs. The lowest-energy MO has zero nodes, the next has one node, and so on. These pi MOs have six electrons. The lowest-energy arrangement of electrons, called the **ground state,** has these six electrons in the three bonding pi MOs. (Any other arrangement of electrons is higher in energy and is termed an **excited state.**) For the ground state of 1,3,5-hexatriene the HOMO is π_3 and the LUMO is π_4*.

As described in the discussion of UV-visible spectroscopy in Section 15.1, the absorption of a photon of light by a compound causes an electron to be excited from an occupied MO to an unoccupied MO. The lowest-energy excitation occurs when an electron in the HOMO is excited to the LUMO. In the case of 1,3,5-hexatriene an electron in π_3 is promoted to π_4* to form the lowest-energy excited state (see Figure 22.3). In the excited state, the HOMO is π_4* and the LUMO is π_5*. It is this excited state that reacts in a photochemical reaction.

Conjugated carbocations, carbanions, and radicals that have an odd number of orbitals are also important. The same rules are used to construct the MOs for these odd orbital systems. As a simple example, consider the allyl radical, shown in Figure 22.4. The three *p* AOs result in the formation of three pi MOs. For these orbitals to be symmetrically placed about zero energy, one must occur at zero energy. Therefore, the allyl radical has a bonding MO, a nonbonding MO at zero energy, and an antibonding MO. The presence of a nonbonding MO is a characteristic of all odd orbital systems.

Another characteristic feature of odd orbital systems is nodes that pass through atoms. For example, π_2^{nb} of the allyl radical has one node. For this node to be symmetrically placed in the radical, it must pass through C-2, as shown in Figure 22.4. This means that the *p* orbital on C-2 does not contribute to the nonbonding MO at all. The *p* orbitals on C-1 and C-3 are too far apart to interact, so this MO has the same energy as an isolated *p* orbital and is nonbonding.

The allyl radical has three electrons, so two occupy π_1 and one occupies the nonbonding MO. The allyl cation and the allyl anion have exactly the same MOs. The

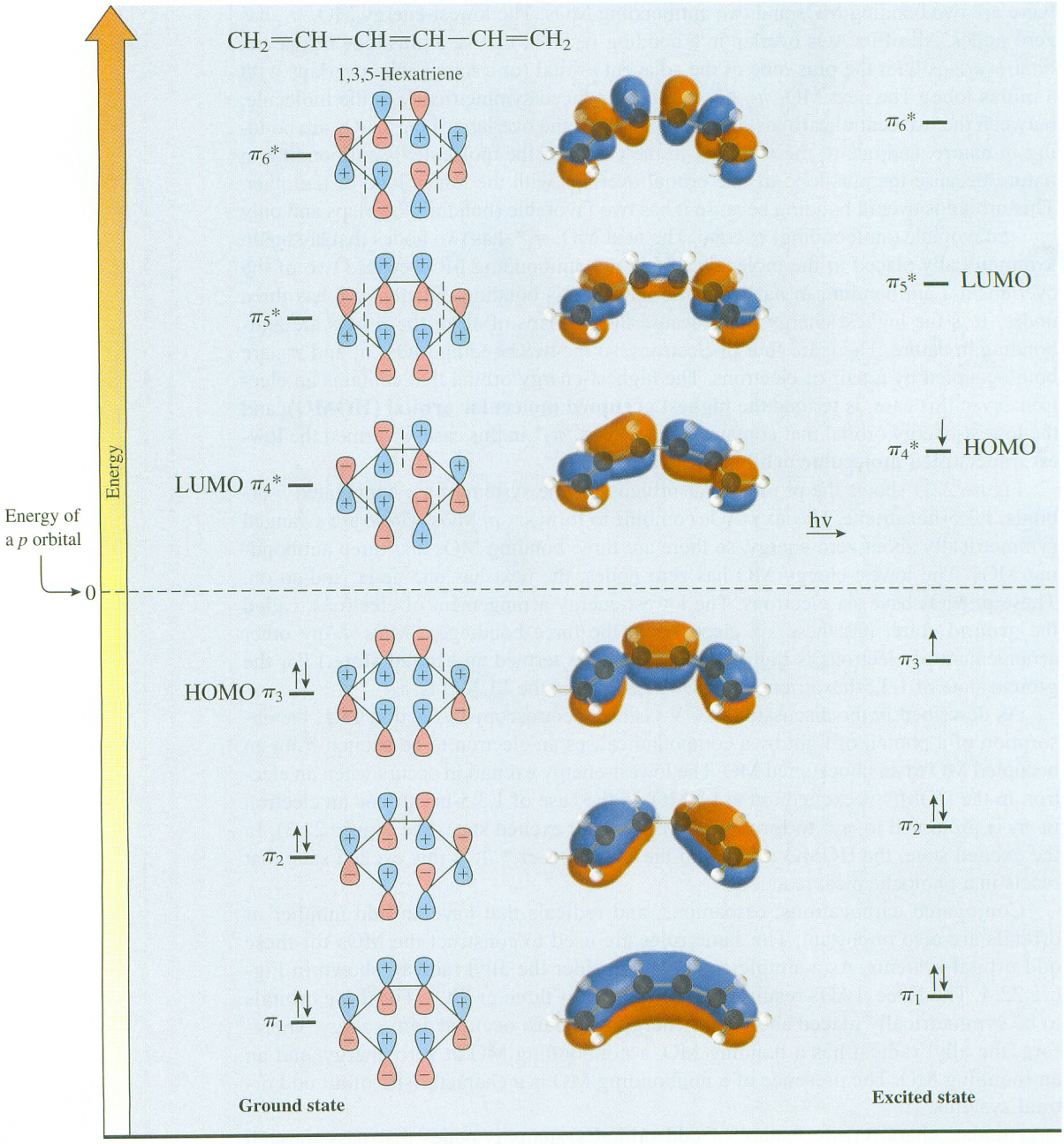


Figure 22.3

ENERGIES AND NODAL PROPERTIES OF THE PI MOS FOR THE GROUND STATE AND THE EXCITED STATE OF 1,3,5-HEXATRIENE.

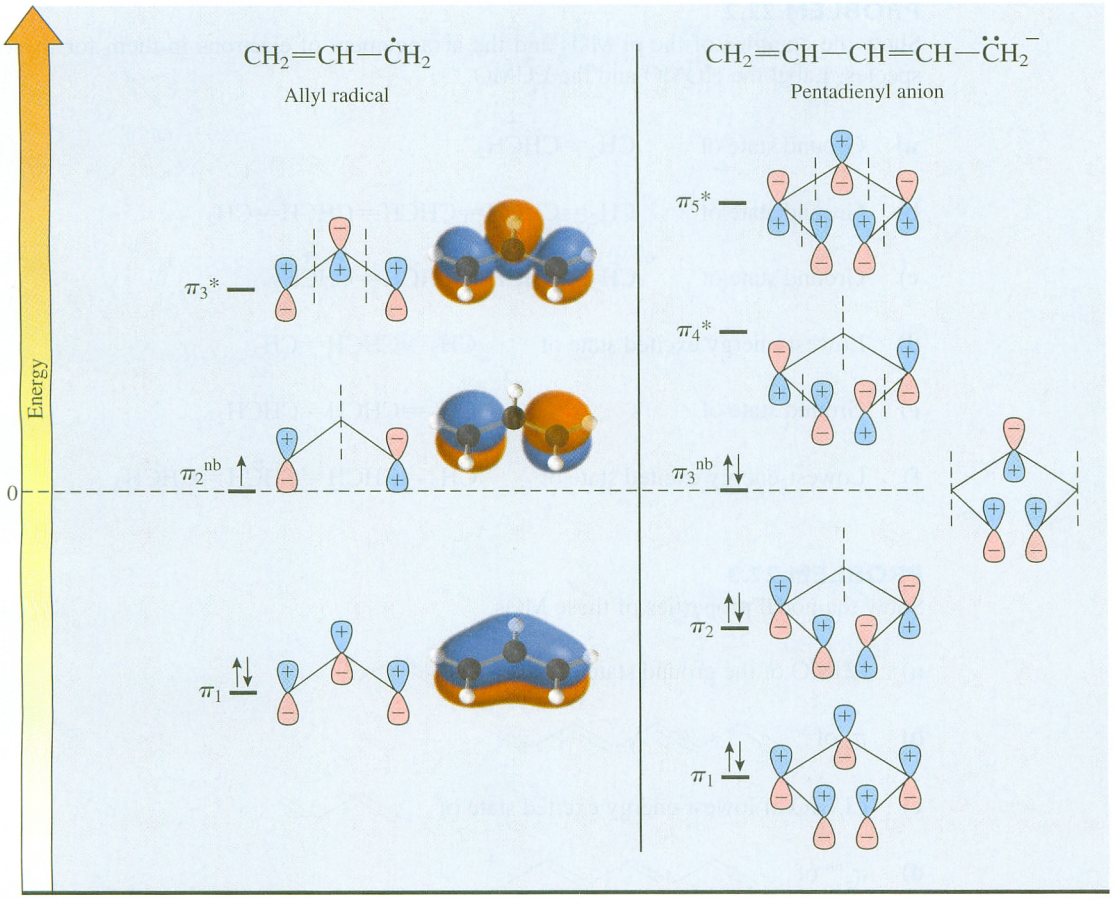


Figure 22.4

ENERGIES AND NODAL PROPERTIES FOR THE PI MOS OF THE ALLYL RADICAL AND THE PENTADIENYL ANION.

cation, however, has only two electrons, which occupy π_1, whereas the anion has four electrons, which fill both the bonding MO and the nonbonding MO.

Figure 22.4 also shows the MOs for the pentadienyl anion. The five *p* orbitals of this carbanion combine to form five MOs: two bonding MOs, two antibonding MOs, and one nonbonding MO. The lowest-energy MO, π_1, has no nodes. The next MO, π_2, has one node that passes through the center of the carbanion at C-3. The nonbonding MO, π_3^{nb}, has two nodes, at C-2 and C-4. The next MO, π_4^*, has three nodes, one of which passes through the center of the molecule at C-3. Finally, π_5^* has four nodes. There are six electrons in this carbanion, so the nonbonding MO is occupied by a pair of electrons.

In general, these odd orbital systems all have a nonbonding MO that has nodes passing through the even-numbered carbons. A cation has no electrons in the nonbonding MO, the radical has one electron in this MO, and the anion has two electrons occupying this MO.

PROBLEM 22.2

Show the energies of the pi MOs and the arrangement of electrons in them for these species. Label the HOMO and the LUMO.

a) Ground state of $CH_2{=}CH\overset{+}{C}H_2$

b) Ground state of $CH_2{=}CHCH{=}CHCH{=}CHCH{=}CH_2$

c) Ground state of $CH_2{=}CHCH{=}CHCH{=}\overset{+}{C}HCH_2$

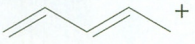
d) Lowest-energy excited state of $CH_2{=}CHCH{=}CH_2$

e) Ground state of $CH_2{=}CHCH{=}C\dot{H}CH_2$

f) Lowest-energy excited state of $CH_2{=}CHCH{=}CHCH{=}C\ddot{H}\ddot{C}H_2^{-}$

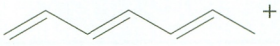
PROBLEM 22.3

Show the nodal properties of these MOs.

a) LUMO of the ground state of 

b) π_2 of

c) LUMO of lowest-energy excited state of

d) π_4^{nb} of 

e) HOMO of the ground state of

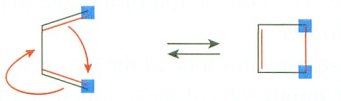
To determine whether a pericyclic reaction is favorable, we need to evaluate how the total energy of the electrons changes during the course of the reaction. As the reaction occurs, the MOs of the reacting molecule are converted into the MOs of the product. If this conversion is energetically favorable—that is, if the electrons in the occupied MOs do not increase in energy—then the reaction is likely to occur and is said to be *allowed*. If the electrons in the occupied MOs increase in energy, the reaction is unfavorable and is said to be *forbidden*. Therefore, we need to evaluate what happens to the energies of the occupied MOs as the reaction proceeds.

The method developed by Woodward and Hoffmann uses the symmetry of the placement of the nodes in the MOs to determine how the reactant MOs are converted to the product MOs and how the total electron energy changes during the course of the reaction. Fukui's method concentrates on the so-called **frontier MOs**, the HOMO and the LUMO, because the energy changes of these are the key to whether the overall energy change is favorable. This method examines how the orbitals of the HOMO, or in some cases the orbitals of the HOMO of one component and the LUMO of the other, overlap to form the new bonds. If the new overlaps are favorable (bonding overlaps),

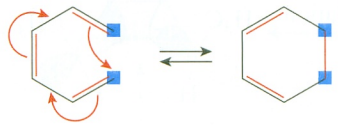
then the reaction is allowed. And if the new overlaps are unfavorable (antibonding overlaps), then the reaction is forbidden. Fukui's method (the **frontier orbital method**) is a little simpler, so it is used in this book. The examples presented in the following sections illustrate how this method is applied.

22.3 Electrocyclic Reactions

Pericyclic reactions are commonly divided into three classes: electrocyclic reactions, cycloaddition reactions, and sigmatropic rearrangements. An **electrocyclic reaction** forms a sigma bond between the end atoms of a series of conjugated pi bonds within a molecule. The 1,3-butadiene to cyclobutene conversion is an example, as is the similar reaction of 1,3,5-hexatriene to form 1,3-cyclohexadiene:



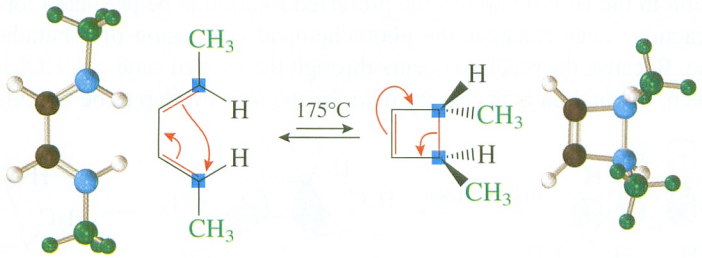
1,3-Butadiene Cyclobutene



1,3,5-Hexatriene 1,3-Cyclohexadiene

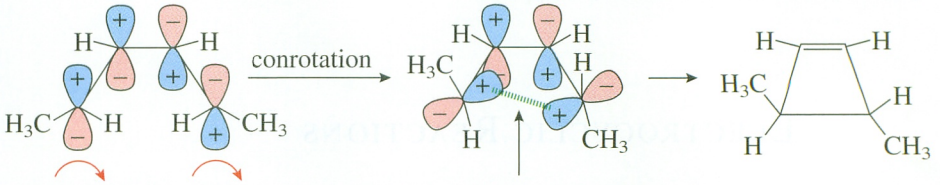
As can be seen from these examples, the product has one more sigma bond and one less pi bond than the reactant.

Let's begin by considering the simplest electrocyclic reaction, the thermally induced interconversion of a diene and a cyclobutene. As illustrated in the following example, the reaction is remarkably stereospecific, occurring only by a conrotatory motion:



In electrocyclic reactions the end carbons of the conjugated system must rotate for the *p* orbitals on these carbons to begin to overlap to form the new carbon–carbon sigma bond. The preference for the stereochemistry of the rotation in these reactions can be understood by examination of the new orbital overlap in the HOMO as the rotation occurs. For the formation of the new sigma bond to be favorable, rotation must occur so that the overlap of the orbitals forming this bond is bonding in the HOMO.

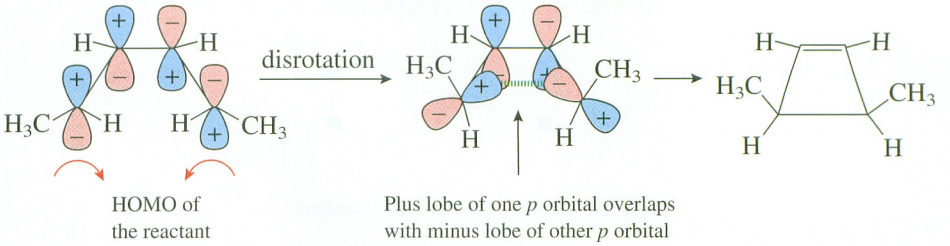
For the ground-state reaction of a conjugated diene the HOMO is π_2. Conrotation of this MO causes the plus lobe of the *p* orbital on one end of the pi system to overlap with the plus lobe of the *p* orbital on the other end of the pi system:



Conrotation of a diene is thermally allowed.

This bonding overlap in the HOMO when the rotation occurs makes the formation of the new sigma bond favorable. The conversion of a diene to a cyclobutene by a conrotatory motion is *thermally allowed*.

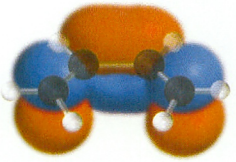
In contrast, disrotation causes the plus lobe of the *p* orbital on one end of the pi system of the diene to overlap with the minus lobe of the *p* orbital on the other end in the HOMO:

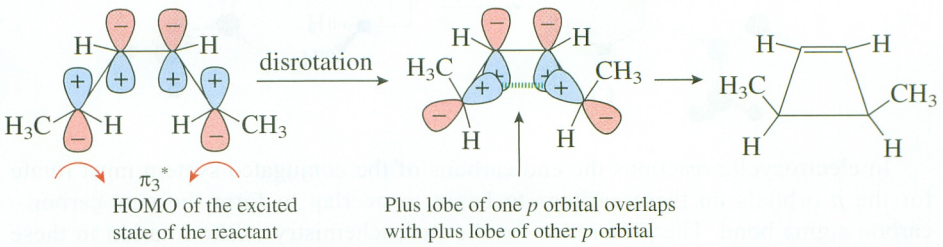


Disrotation of a diene is thermally forbidden.

The antibonding overlap in the HOMO when disrotation occurs makes the formation of the new sigma bond unfavorable. The disrotatory closure of a diene to a cyclobutene is *thermally forbidden*.

The requirement for a favorable bonding overlap of the orbitals forming the new sigma bond in the HOMO allows the preferred rotation to be predicted for any electrocyclic reaction. Let's consider the photochemical conversion of a butadiene to a cyclobutene. Because the reaction occurs through the excited state, the HOMO is π_3^*. As can be seen, disrotation is necessary here for the new overlap to be bonding:




disrotation
HOMO of the excited state of the reactant
Plus lobe of one p orbital overlaps with plus lobe of other p orbital

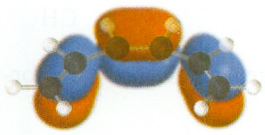
Disrotation of a diene is photochemically allowed.

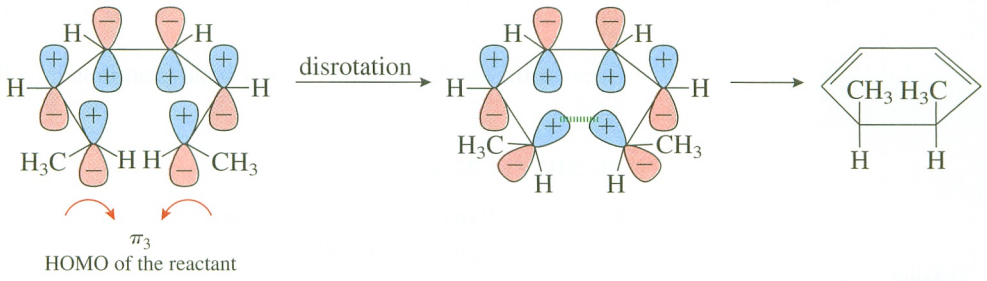
In accord with this analysis, numerous experiments have shown that the disrotatory closure of a diene to a cyclobutene is indeed the pathway that occurs when the compound is irradiated with UV light.

PROBLEM 22.4

Use orbital drawings to show that conrotation of a diene is photochemically forbidden.

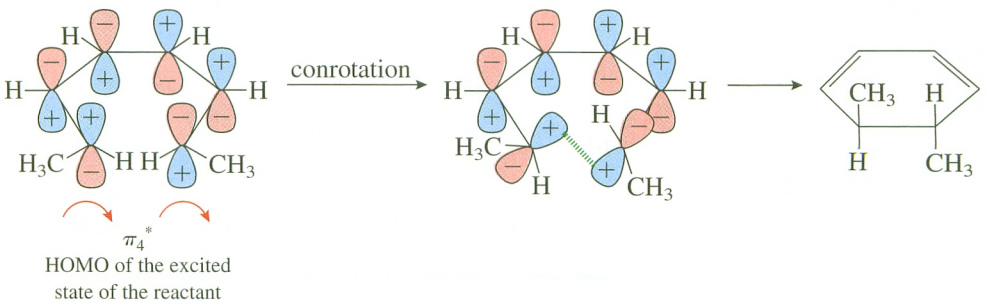
A similar analysis also correctly predicts the stereochemistry of the formation of a cyclohexadiene from a triene. For the thermal reaction the HOMO is π_3. Examination of this MO shows that disrotation is necessary for the overlap forming the new sigma bond to be bonding:





Disrotation of a triene is thermally allowed.

For the excited state reaction the HOMO is π_4*. Here conrotation is the favored pathway:

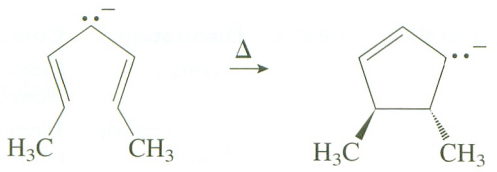


Conrotation of a triene is photochemically allowed.

Both of these conclusions are in accord with the experimental results presented in the next section.

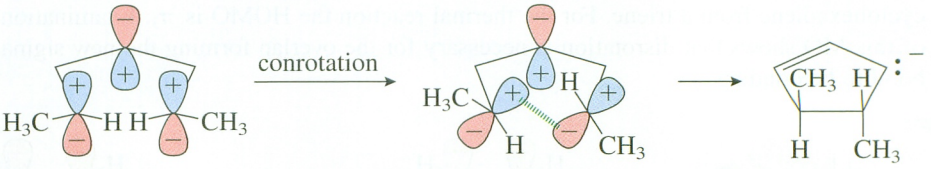
PRACTICE PROBLEM 22.1

Use orbital drawings to determine whether this reaction is allowed or forbidden:



Solution

This anion has five *p* orbitals, so there are five MOs (see Figure 22.4). There are six electrons in these MOs, so the HOMO for the thermal (ground state) reaction is π_3^{nb}. Conrotation is necessary to form the product with the methyl groups trans.



Because the overlap to form the new bond is antibonding, this reaction is thermally forbidden.

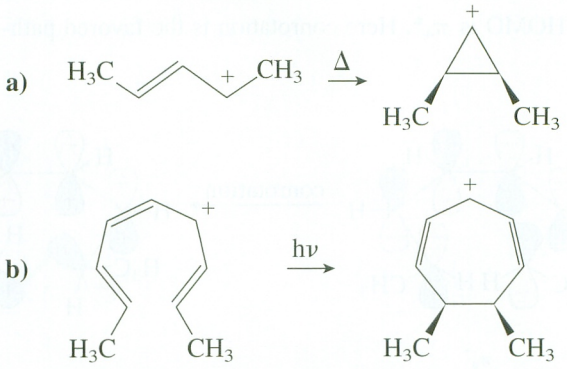
PROBLEM 22.5

Use orbital drawings to show that conrotation of a triene is thermally forbidden and that disrotation is photochemically forbidden.

ORGANIC Chemistry Now™
Click *Coached Tutorial Problems* for more practice using MOs to predict the stereochemistry of **Electrocyclic Reactions.**

PROBLEM 22.6

Use orbital drawings to determine whether these reactions are allowed or forbidden:



It is possible to generalize the preferences for conrotation or disrotation based on the number of electron pairs in the pi MOs of the reacting molecule. A diene, with two pi electron pairs (two pi bonds), has π_2 as its HOMO in the ground state. Because this MO has one node, conrotation is favored for the thermal reaction. A triene, with three pi electron pairs (three pi bonds), has π_3 as its HOMO. This MO has two nodes (one more than π_2 of a diene), so the opposite rotation, disrotation, is preferred. It is apparent that the favored rotation alternates with the number of pi electron pairs. Therefore, a molecule with four pi bonds (π_4 is the HOMO) prefers conrotation. Furthermore, the preference for the excited state is just reversed from that of the ground state because the excited-state HOMO always has one more node than the ground-state HOMO. These preferences are summarized in the following chart:

Number of Electron Pairs	Disrotation	Conrotation
Odd	Thermally allowed	Photochemically allowed
Even	Photochemically allowed	Thermally allowed

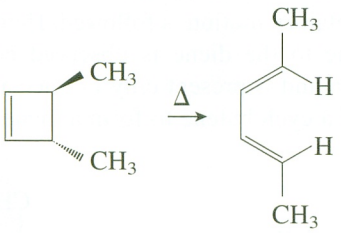
(Note that an odd number of electron pairs equals $4n + 2$ electrons, whereas an even number of electron pairs equals $4n$ electrons, where n is any integer, including zero.)

PROBLEM 22.7

Use the preceding chart to determine whether the reactions of problem 22.6 are allowed or forbidden.

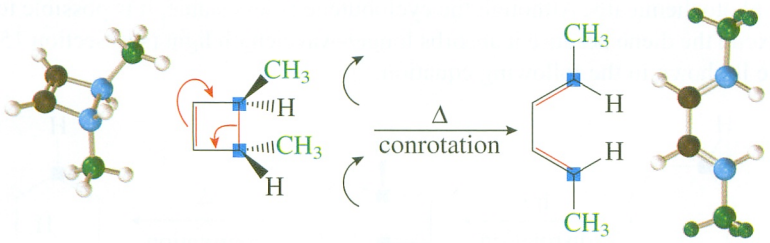
PRACTICE PROBLEM 22.2

Determine the number of electron pairs in this reaction, the type of rotation, and whether the reaction is allowed or forbidden:



Solution

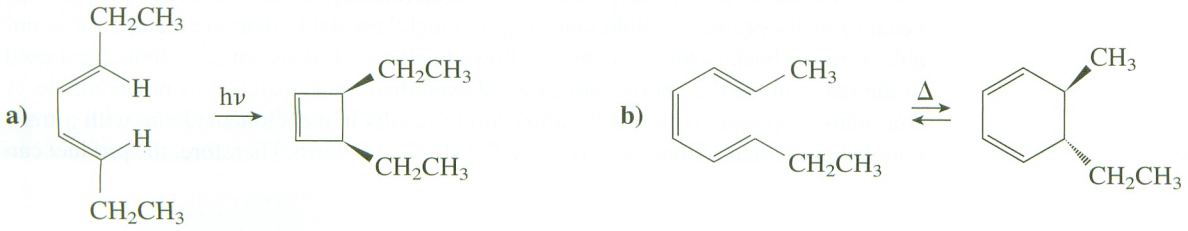
We have usually analyzed this type of reaction from the other direction—that is, the conversion of a diene to a cyclobutene. However, the same analysis works for either direction of a reaction. In this case an even number (two) of electron pairs are involved; the sigma bond and the pi bond of the reactant are converted to the two pi bonds of the product. The reaction occurs by a conrotation:

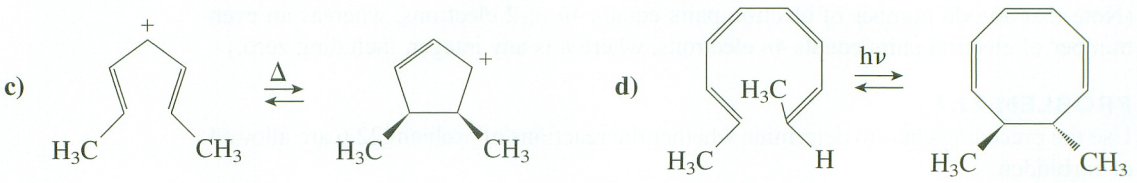


According to the chart, a conrotation involving an even number of electron pairs is thermally allowed. Therefore, the reaction shown is allowed. Note that the same reaction is forbidden under photochemical conditions.

PROBLEM 22.8

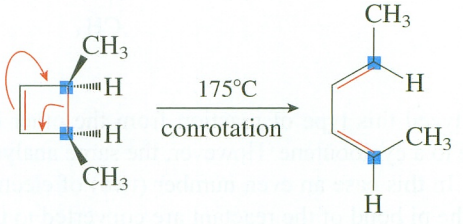
Indicate the number of electron pairs and the type of rotation for these reactions and determine whether each is allowed or forbidden:



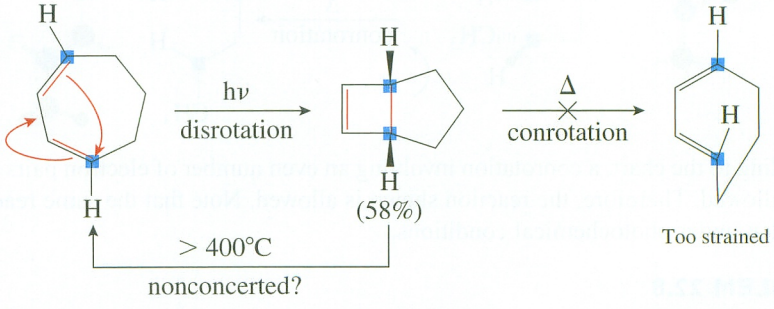


22.4 Examples of Electrocyclic Reactions

The analysis in Section 22.3 indicates that the thermal interconversion of a diene with a cyclobutene should occur by conrotation. The reaction is allowed in both directions, as long as a conrotatory motion is followed. However, usually only the conversion of the cyclobutene to the diene is observed because the cyclobutene is destabilized by angle strain and is present only in trace amounts at equilibrium. An example of the opening of a cyclobutene to form a diene is provided by the following equation:



The reverse process, the conversion of a diene to a cyclobutene, can be accomplished photochemically. Although the cyclobutene is less stable, it is possible to selectively excite the diene because it absorbs longer-wavelength light (see Section 15.2). An example is shown in the following equation:

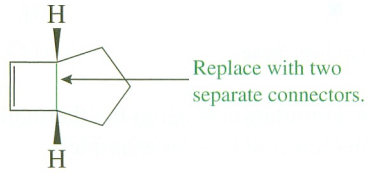


In this reaction, light of appropriate energy is used to selectively excite 1,3-cycloheptadiene. The diene closes to a cyclobutene by a disrotatory motion. Although the product, because of its strained cyclobutene ring, is much less stable than the reactant, it is unable to revert back to the diene by an allowed pathway. It does not absorb the light used in the reaction, so the photochemically allowed disrotatory pathway is not available. A conrotatory opening is thermally allowed but results in a cycloheptadiene with a trans double bond. Such a compound is much too strained to form. Therefore, the product can

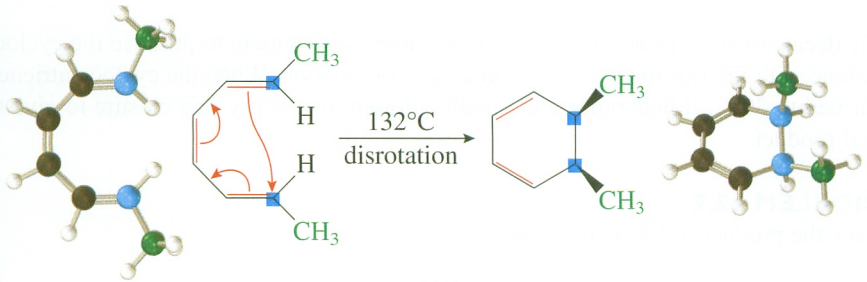
be readily isolated. If it is heated to a high enough temperature, greater than 400°C, the strained ring does break to produce 1,3-cycloheptadiene. This reaction might be occurring by the forbidden disrotatory pathway, or, more likely, it may involve a nonconcerted mechanism.

MODEL BUILDING PROBLEM 22.2

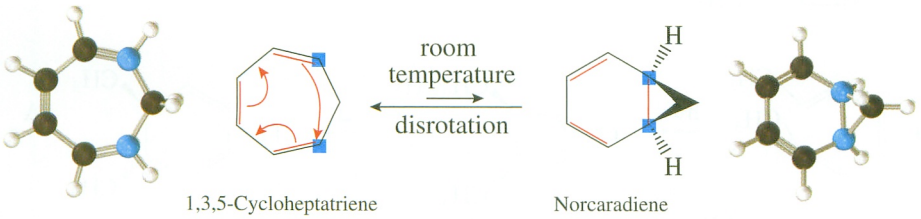
Build a model of the following compound. Then replace the connector for the bond that is part of both rings with two separate connectors. Do a conrotation and a disrotation to see the strain that is incurred in each process.



The thermally allowed cyclization of a triene to form a cyclohexadiene occurs by a disrotatory motion, as illustrated in the following equation. In this case the product is favored at equilibrium because it has one more sigma bond and one fewer pi bond than the reactant. (Sigma bonds are stronger than pi bonds.)



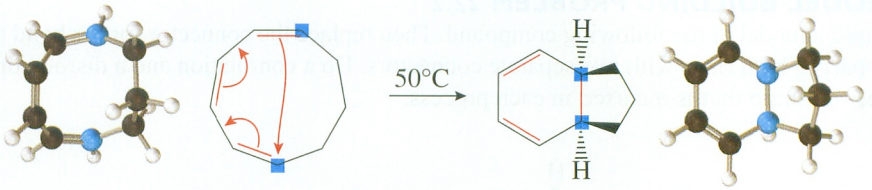
As another example, the electrocyclic interconversion of 1,3,5-cycloheptatriene and norcaradiene also occurs by a disrotatory motion:



1,3,5-Cycloheptatriene Norcaradiene

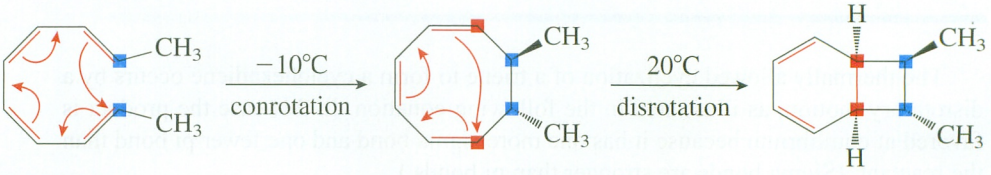
Norcaradiene cannot be isolated because its conversion to cycloheptatriene is fast at room temperature and its concentration in the equilibrium mixture is very low be-

cause of ring strain. In a related example, 1,3,5-cyclononatriene cyclizes by a disrotatory motion, as shown in the following equation. Again, the reaction is quite facile, as illustrated by its half-life of about 1 h at 50°C. In this case the product, with a five- and a six-membered ring, is more stable than the starting material with its nine-membered ring:



1,3,5-Cyclononatriene (100%)

In the case of a tetraene, conrotation is again the thermally allowed pathway for cyclization. The following equation provides an example:

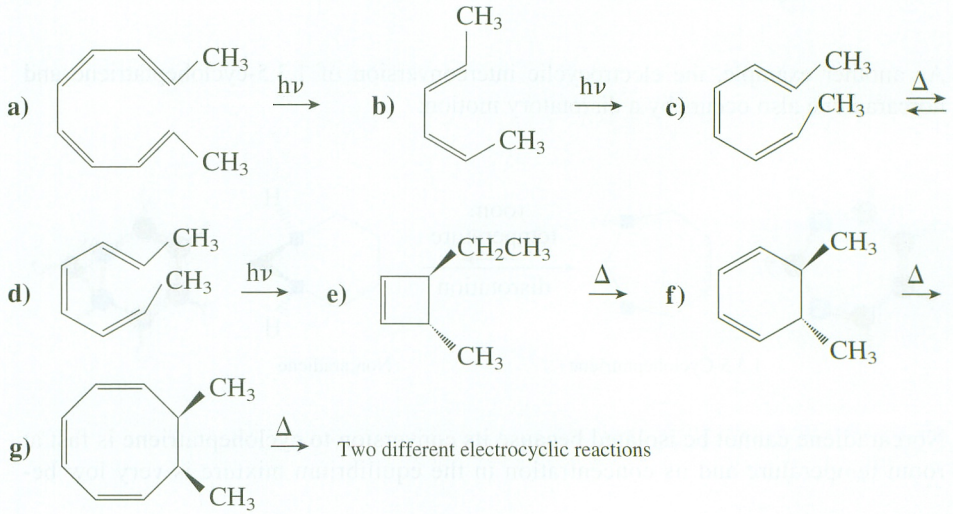


Decatetraene Cyclooctatriene (100%)

The decatetraene cyclizes at −10°C, by a conrotatory motion, to produce the cyclooctatriene with the two methyl groups in a trans orientation. When the cyclooctatriene is warmed to 20°C, it undergoes a thermally allowed disrotatory ring closure to give the final product.

PROBLEM 22.9

Show the products of these reactions:

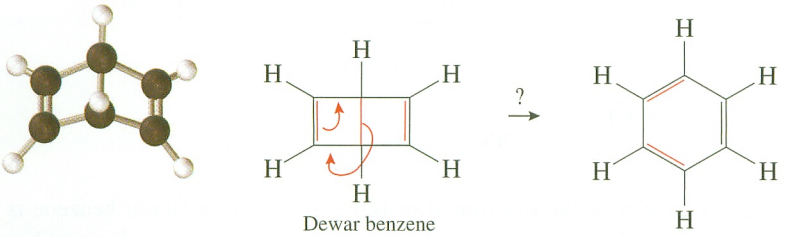


Two different electrocyclic reactions

Focus On

Dewar Benzene

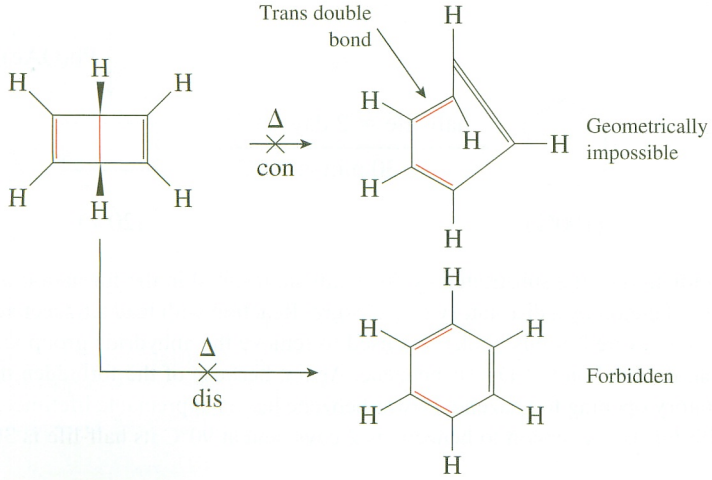
In the mid-1800s, chemists were struggling to determine the structure of benzene. One of the structures that was proposed at that time is known as Dewar benzene, after the chemist who suggested it:



Dewar benzene

As chemists learned more about the effects of structure on the stability of organic compounds, it became apparent that Dewar benzene is much less stable than benzene. Not only does it have a considerable amount of angle strain, but it also has none of the stabilization due to aromaticity that benzene has. Because of these factors, Dewar benzene is 71 kcal/mol (297 kJ/mol) less stable than benzene. Because the conversion of Dewar benzene to benzene is so exothermic and involves an apparently simple electron reorganization, many chemists believed that the isolation of this strained isomer would prove to be impossible. They thought that if it were prepared, it would rapidly convert to benzene. In support of this view, numerous attempts to synthesize Dewar benzene met with failure.

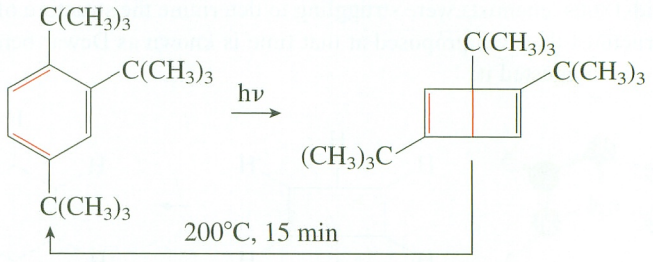
Once the theory of pericyclic reactions was developed, it was recognized that the conversion of Dewar benzene to benzene is an electrocyclic reaction. This conversion involves two pairs of electrons: one pair of pi electrons and one pair of sigma electrons of the Dewar benzene. (The third pair of electrons is located in exactly the same place in both the reactant and the product and so is not involved in the reaction.) An electrocyclic reaction involving two pairs of electrons must occur by a conrotatory motion if it is to be thermally allowed. However, the conrotatory opening of Dewar benzene is geometrically impossible, because it would result in a benzene with a trans double bond, a compound with too much angle strain to exist.



Continued

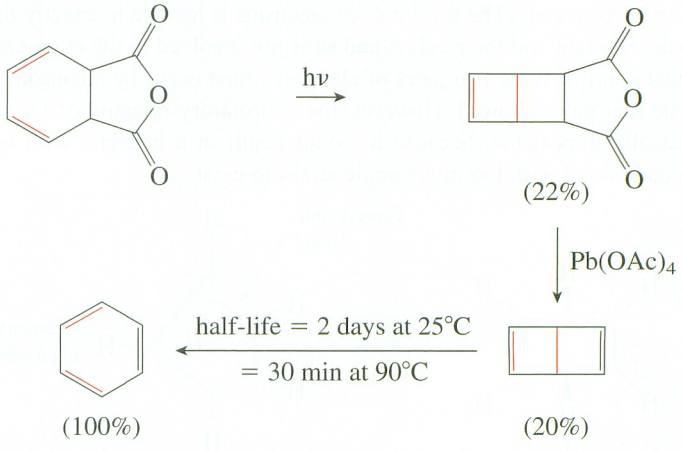
Disrotatory opening of Dewar benzene, which would produce benzene, is thermally forbidden. Therefore, even though the conversion of Dewar benzene to benzene is quite exothermic, it might indeed prove possible to isolate Dewar benzene because there is no low-energy pathway for its conversion to benzene.

The first derivative of Dewar benzene was prepared in 1962 by irradiation of 1,2,4-tri-*t*-butylbenzene:



Disrotatory closure of the substituted benzene to produce a Dewar benzene is photochemically allowed, as is, of course, the reverse process. However, because benzene is conjugated, it absorbs UV light at longer wavelengths than the Dewar benzene isomer. Therefore, it is possible to selectively excite the benzene chromophore and produce the less stable Dewar isomer. In this particular case the *tert*-butyl groups favor the reaction because they destabilize the benzene isomer somewhat, owing to steric hindrance. Because the two adjacent *tert*-butyl groups in the Dewar isomer do not lie in the same plane, this steric strain is decreased in the product. Because of this steric effect and the forbidden nature of the conversion back to benzene, the Dewar isomer is relatively stable. However, when it is heated to 200°C, it is rapidly converted to the benzene isomer, probably by a nonconcerted pathway.

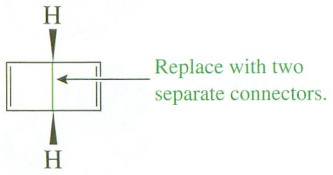
Shortly after this, in 1963, the parent Dewar benzene was prepared by the following reaction sequence:



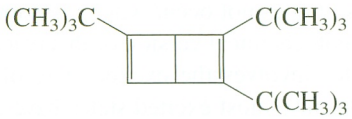
Irradiation of the substituted cyclohexadiene resulted in the formation of the Dewar benzene skeleton by a disrotatory ring closure. Reaction with lead tetraacetate (a reaction that is not covered in this book) was used to remove the anhydride group and introduce the final double bond of Dewar benzene. Again, because of the forbidden nature of the conrotatory opening to benzene, Dewar benzene has an appreciable lifetime. At 25°C the half-life for its conversion to benzene is 2 days, and at 90°C its half-life is 30 min.

MODEL BUILDING PROBLEM 22.3

Build a model of Dewar benzene. Then replace the connector for the bond that is part of both rings with two separate connectors. Do a conrotation and a disrotation to see the strain that is incurred in each process. Also build a model of 1,2,4-tri-*t*-butylbenzene and the Dewar benzene formed from it and examine the steric strain that is present in each compound.

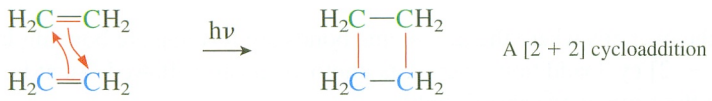


Explain why the following Dewar benzene is not produced in the photochemical reaction of 1,2,4-tri-*t*-butylbenzene:

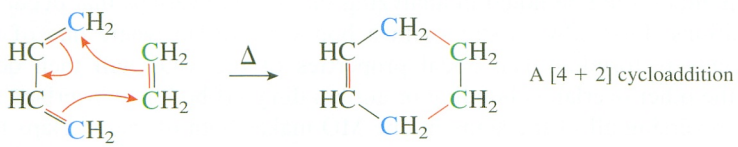


22.5 Cycloaddition Reactions

A **cycloaddition reaction** most commonly involves two molecules reacting to form two new sigma bonds between the end atoms of their pi systems, resulting in the formation of a ring. The product has two more sigma bonds and two fewer pi bonds than the reactants. The reactions are classified according to the number of pi electrons in each of the reactants. Thus, the reaction of two alkenes to form a cyclobutane derivative is termed a [2 + 2] cycloaddition reaction, and the reaction of a diene with an alkene to form a cyclohexene derivative is termed a [4 + 2] cycloaddition reaction:



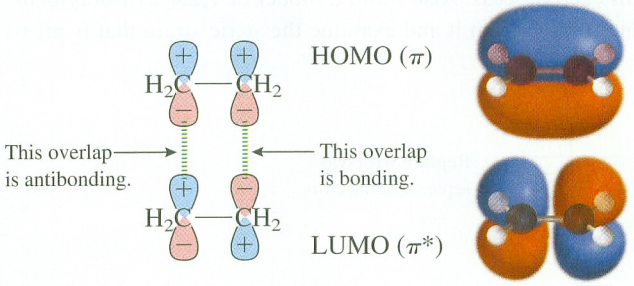
A [2 + 2] cycloaddition



A [4 + 2] cycloaddition

Cycloaddition reactions can be viewed as involving the flow of electrons from the HOMO of one reactant to the LUMO of the other. Therefore, examination of the interaction of these MOs is used to determine whether the reaction is favorable. For a cycloaddition to be allowed, the overlap of the orbitals of the HOMO of one component and the LUMO of the other must be bonding where the new sigma bonds are to be formed. Some examples will help make the application of this rule clear.

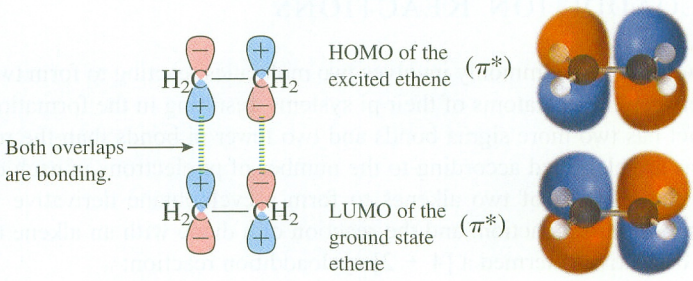
Let's consider first the thermal [2 + 2] cycloaddition. The overlaps between the HOMO of one component (π) and the LUMO of the other (π^*) are as follows:



The [2 + 2] cycloaddition is forbidden by a thermal pathway.

Because one of these overlaps is bonding and the other is antibonding, the reaction is thermally forbidden—that is, it does not occur when the compounds are heated.

Next, let's consider the photochemical version of this reaction. A photochemical reaction between two molecules involves the excited state of one component and the ground state of the other. (Because most excited states have extremely short lifetimes, the chances of two excited molecules colliding are exceedingly small, so reactions where both components are excited are highly improbable.) The HOMO of the excited ethene is π^*, and the LUMO of the ground-state ethene is also π^*. The overlaps are as follows:

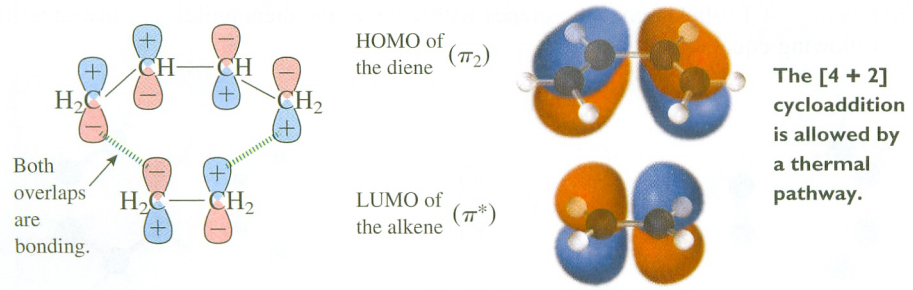


The [2 + 2] cycloaddition is allowed by a photochemical pathway.

Both of the overlaps where the new sigma bonds are forming are bonding interactions, so the [2 + 2] cycloaddition reaction is photochemically allowed—that is, it does occur when the compounds absorb light.

Two points should be noted in analyzing the orbital overlaps that occur in these cycloadditions. First, always start with a bonding overlap where one of the new sigma bonds is forming. The nodal properties of the MOs will then determine whether the other overlap is bonding or antibonding. (If both new overlaps are antibonding, reversing all of the signs in one MO makes both of the overlaps bonding, so the reaction is allowed.) Second, it does not matter whether the analysis is done by employing the HOMO of component A and the LUMO of component B or the LUMO of component A and the HOMO of component B. Both analyses give the same results.

Let's consider the [4 + 2] cycloaddition. The interaction of the HOMO of 1,3-butadiene (π_2) with the LUMO of ethene (π^*) is as follows:


Both overlaps are bonding.
HOMO of the diene (π_2)
LUMO of the alkene (π^*)
The [4 + 2] cycloaddition is allowed by a thermal pathway.

Both overlaps are bonding, so the reaction is thermally allowed.

PROBLEM 22.10

Use orbital drawings to show that the [4 + 2] cycloaddition reaction is photochemically forbidden.

PROBLEM 22.11

Use orbital drawings to determine whether the thermal [4 + 4] cycloaddition reaction is allowed or forbidden.

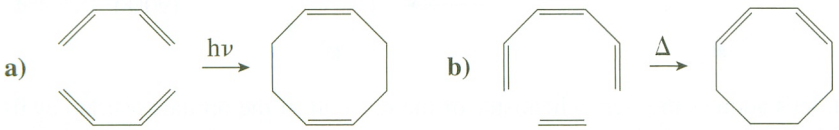
If another pi bond is added to either component of the previous cycloaddition, an additional node is introduced into either the HOMO or the LUMO, resulting in the reaction being thermally forbidden and photochemically allowed. Recognition of this pattern enables the preferences for cycloadditions to be summarized in the chart below.

Number of Electron Pairs	Allowed Cycloaddition
Odd	Thermal
Even	Photochemical

Examples of cycloaddition reactions are presented in the next two sections.

PROBLEM 22.12

Indicate how many electron pairs are involved in these reactions and determine whether each reaction is allowed or forbidden:

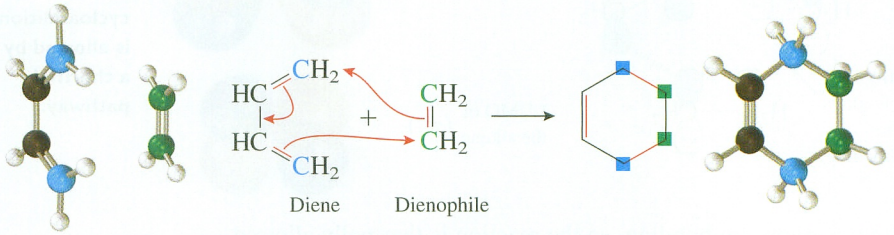


22.6 THE DIELS-ALDER REACTION

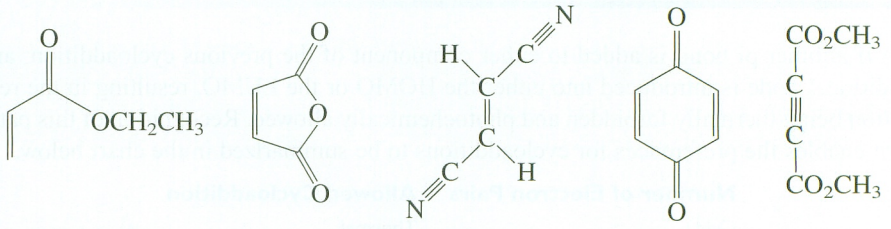
The [4 + 2] cycloaddition was discovered long before the theory of pericyclic reactions was developed. It is more commonly known as the *Diels-Alder reaction,* named after O. Diels and K. Alder, who shared the 1950 Nobel Prize in chemistry for developing this reaction. The Diels-Alder reaction occupies a very important place among the tools of the synthetic organic chemist because it provides a method for the construction of six-membered rings from acyclic precursors with excellent control of stereochemistry.

In general, the Diels-Alder reaction involves the combination of a diene with an alkene, termed a dienophile, to form a cyclohexene derivative. The simplest example,

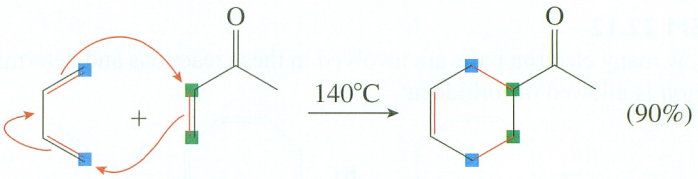
the reaction of 1,3-butadiene (the diene) with ethene (the dienophile), is illustrated in the following equation:



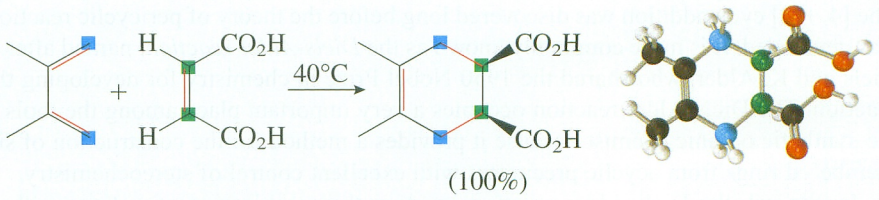
The yield of cyclohexene in this particular reaction is not very high. In general, the yields in the Diels-Alder reaction are much better if the diene and the dienophile are substituted with groups of opposite polarity—that is, with electron-withdrawing groups on one component and electron-donating groups on the other. The vast majority of examples that have been reported have employed electron-withdrawing groups on the dienophile. Some examples of the many alkenes, substituted with electron-withdrawing groups, that are excellent dienophiles in the Diels-Alder reaction are as follows:



The following equation provides an example of the use of a good dienophile in a Diels-Alder reaction that proceeds in excellent yield:

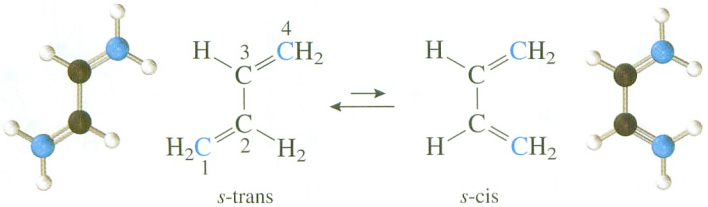


Next, let's address the stereochemistry of the reaction. If the orbitals overlap as illustrated in Section 22.5, the addition is syn on both the diene and the dienophile. An example showing that the addition is indeed syn on the dienophile is illustrated in the following equation. In this reaction the *cis*-stereochemistry of the carboxylic acid groups in the dienophile is preserved in the adduct:



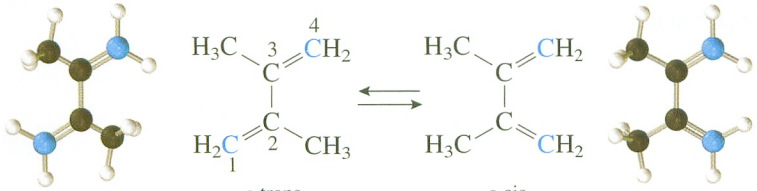
Now let's consider the three-dimensional shape of the diene. To maximize the stabilization due to conjugation, the *p* orbitals on the central carbons of a diene must be

parallel. For an acyclic diene, such as 1,3-butadiene, there are two planar conformations for which these orbitals are parallel:



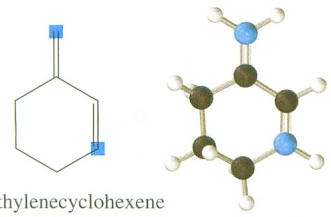
The conformation that has C-1 and C-4 of the double bonds on opposite sides of the single bond between C-2 and C-3 is termed the ***s*-trans conformation,** whereas the conformation that has them on the same side of the single bond is called the ***s*-cis conformation.** The *s*-trans conformation of 1,3-butadiene is more stable because it has less steric strain—the larger groups are farther apart. Although the interconversion of these two conformations is fast, only the *s*-cis conformation can react in the Diels-Alder cycloaddition. In the *s*-trans conformation, C-1 and C-4 are too far apart to bond simultaneously to the dienophile.

The reactivity of a particular diene depends on the concentration of the *s*-cis conformation in the equilibrium mixture. Factors that increase the concentration of this conformation make the diene more reactive. As an example of this effect, consider 2,3-dimethyl-1,3-butadiene:



The methyl groups on C-2 and C-3 cause the *s*-trans and *s*-cis conformations to have similar amounts of steric strain. Therefore, more of the *s*-cis conformer is present at equilibrium for 2,3-dimethyl-1,3-butadiene than for 1,3-butadiene itself. For this reason, 2,3-dimethyl-1,3-butadiene reacts about 10 times faster than 1,3-butadiene in the Diels-Alder reaction.

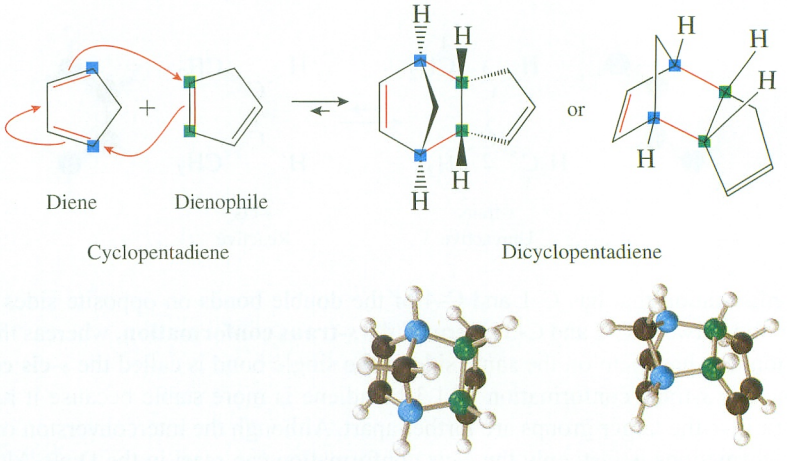
In the case of 3-methylenecyclohexene the double bonds are held in the *s*-trans conformation. This compound cannot react as a diene in the Diels-Alder reaction.



3-Methylenecyclohexene

In contrast, the double bonds of cyclopentadiene are held in the *s*-cis conformation. This makes cyclopentadiene so reactive as a diene in the Diels-Alder reaction that it

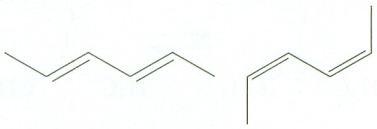
dimerizes at room temperature. One molecule reacts as the diene and the other as the dienophile to form dicyclopentadiene, as shown in the following equation:



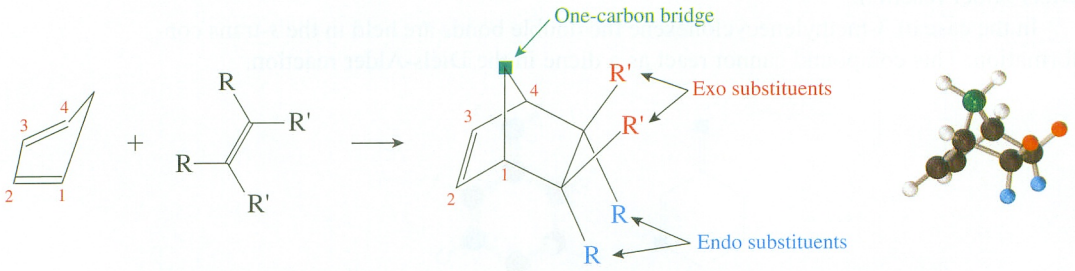
Cyclopentadiene cannot be purchased because it is too reactive and dimerizes to dicyclopentadiene upon storage. If it is needed, it is prepared by heating dicyclopentadiene. Cyclopentadiene is produced in a reverse Diels-Alder reaction. It is distilled from the hot reaction mixture as it is formed and used immediately.

PROBLEM 22.13

Explain which of these isomers of 2,4-hexadiene is more reactive as a diene in the Diels-Alder reaction:

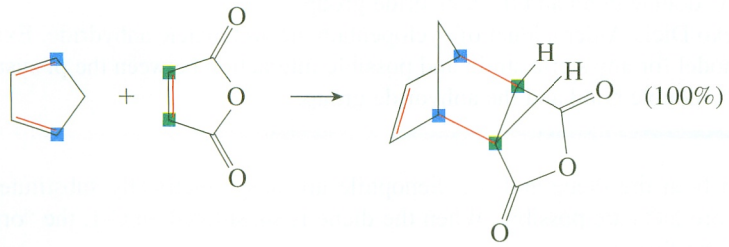


The dimerization of cyclopentadiene introduces a new aspect of the Diels-Alder reaction, the stereochemical relationship between the diene and the dienophile. When cyclopentadiene reacts as a diene, the newly formed six-membered ring of the product has a one-carbon bridge connecting positions 1 and 4:

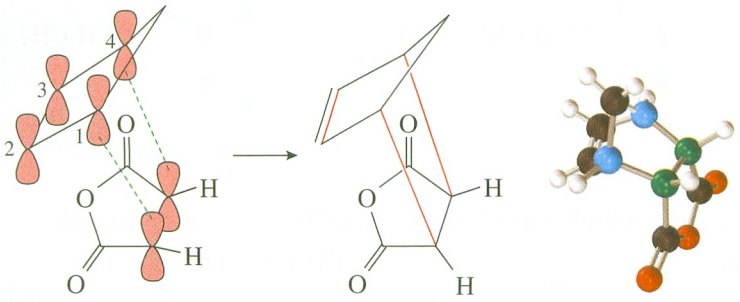


Groups that are cis to this bridge are termed **exo** substituents, and groups that are trans to this bridge are termed **endo** substituents.

The dicyclopentadiene that is formed in the dimerization of cyclopentadiene has the ring of the dienophile in an endo orientation to the cyclopentadiene ring that acts as the diene. Usually, substituents on the dienophile are found to be endo in the adduct if the substituents contain pi bonds. Another example is provided by the reaction of cyclopentadiene and maleic anhydride illustrated in the following equation:

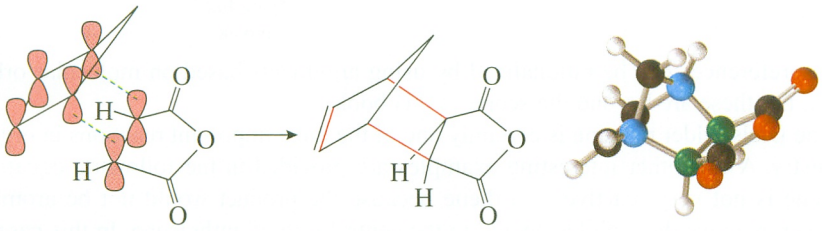


The orientation of the reactants that leads to the endo product is as follows:



Endo adduct
(observed)

and the orientation that leads to the exo product is as follows:



Exo adduct
(not observed)

(Models may be useful to help you visualize these different orientations.) Because the orientation leading to the endo adduct is more sterically congested than that leading to the exo adduct, it is apparent that steric effects are not controlling the orientation. Rather, it appears that a stabilizing interaction between the orbitals on C-2 and C-3 of the diene with pi orbitals on the substituents of the dienophile causes the endo orientation to be preferred. As a result, the group with the *p* orbitals prefers to be cis to the double bond bridge and trans to the one-carbon bridge.

MODEL BUILDING PROBLEM 22.4

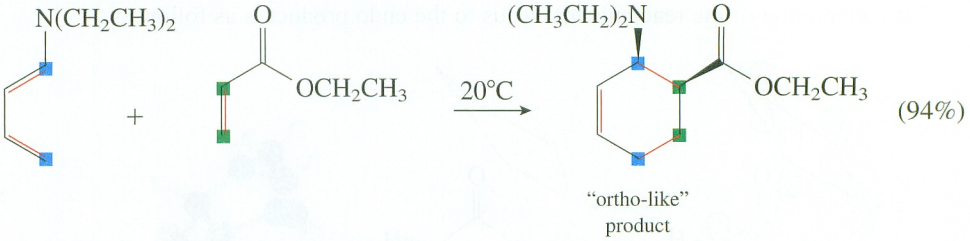
Build these models:

a) The Diels-Alder adduct of ethene and cyclopentadiene. Identify the exo and endo positions.

b) The endo Diels-Alder adduct of cyclopentadiene and maleic anhydride. Examine the model for any steric strain and possible interaction between the pi systems of the CC double bond and the anhydride group.

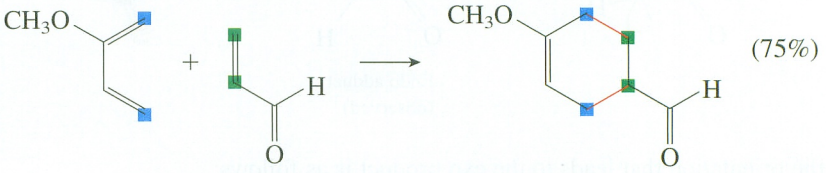
c) The exo Diels-Alder adduct of cyclopentadiene and maleic anhydride. Examine the model for any steric strain and possible interaction between the pi systems of the CC double bond and the anhydride group.

When both the diene and the dienophile are unsymmetrically substituted, regioisomeric products are possible. When the diene is substituted on C-1, the "ortho-like" product is preferred:



"ortho-like" product

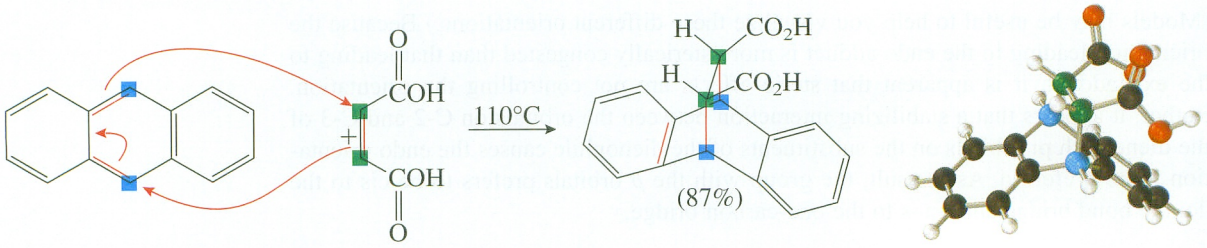
When the diene is substituted on C-2, the "para-like" product is preferred.



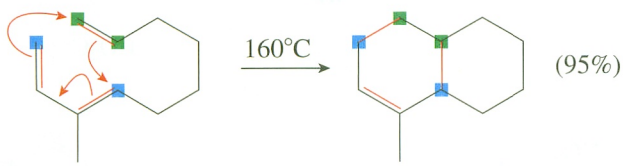
"para-like" product

These preferences can be rationalized by using arguments based on molecular orbital theory, but these are beyond the scope of this book.

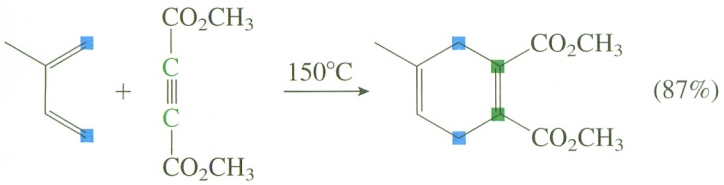
The Diels-Alder reaction is certainly one of the most important reactions in organic chemistry. A few other interesting examples are provided in the following equations. Benzene is not very reactive as a diene because the product would not be aromatic. However, reactive dienophiles do add to the central ring of anthracene. In this case the product, with two benzene rings, has not lost much aromatic resonance energy.



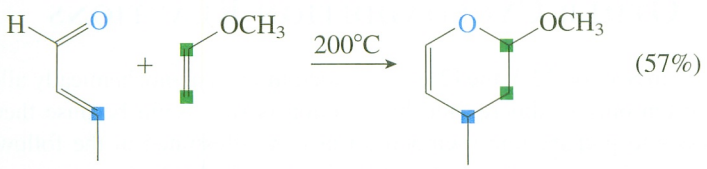
Intramolecular Diels-Alder reactions can be used to construct several rings simultaneously:



The dienophile can be an alkyne:



Atoms other than carbon can even be part of the diene or dienophile:



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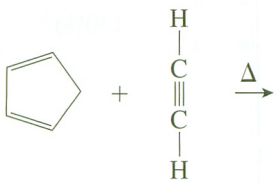
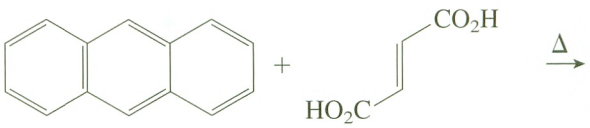
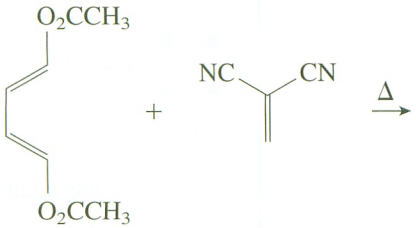
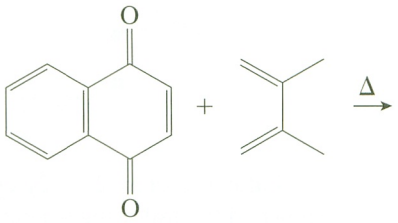
Click *Coached Tutorial Problems* to practice additional **Diels-Alder Reactions.**

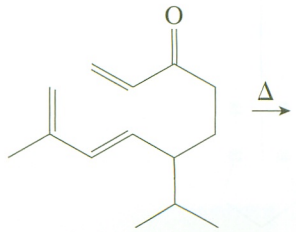
PROBLEM 22.14
Show the products of these reactions.

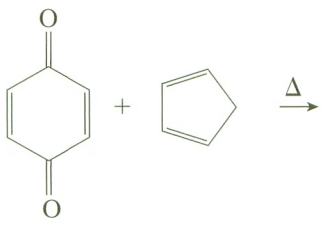
a) 

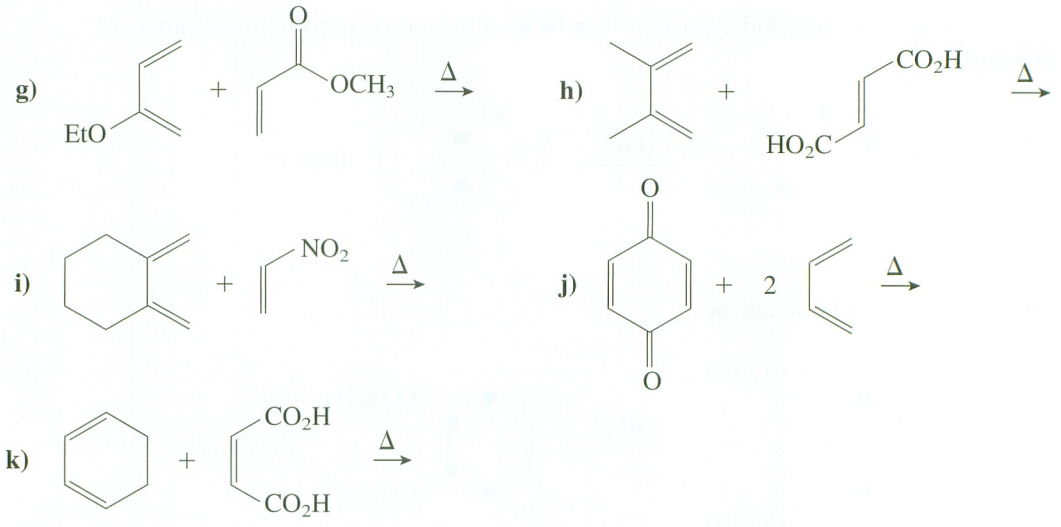
b) 

c) 

d) 

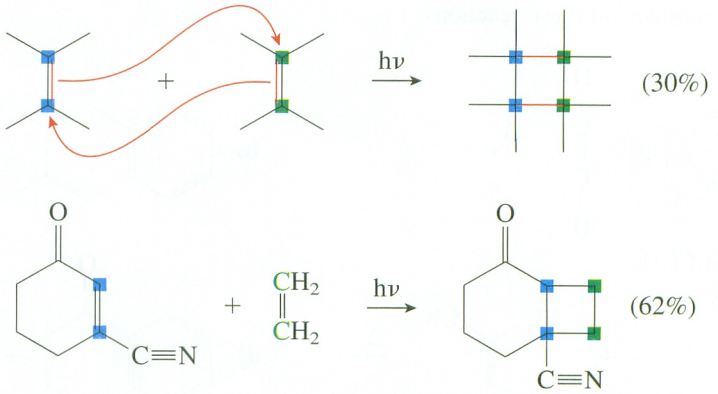
e) 

f) 

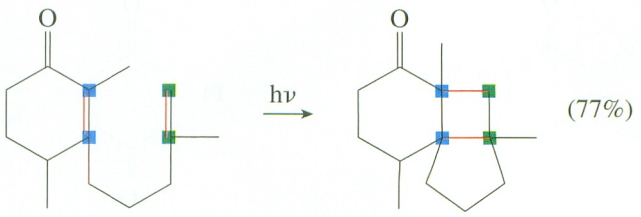


22.7 Other Cycloaddition Reactions

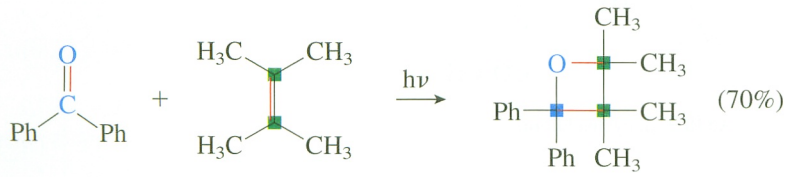
As discussed in Section 22.5, the [2 + 2] cycloaddition is photochemically allowed. The yields are often only mediocre, but this reaction is still useful because there are few good methods to prepare four-membered rings. As illustrated in the following equations, the cycloaddition can be used to dimerize two identical alkenes or to cyclize different alkenes:



Intramolecular [2 + 2] cycloadditions often give good yields of the adduct, as shown in the following example:

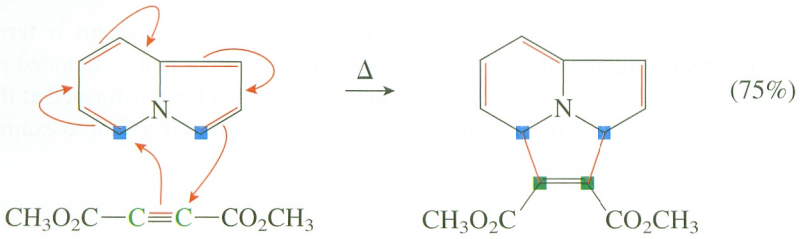


The CO double bond of an aldehyde or a ketone can act as one component in a [2 + 2] cycloaddition with an alkene. The product, a four-membered ring containing an oxygen, is called an oxetane.



An oxetane

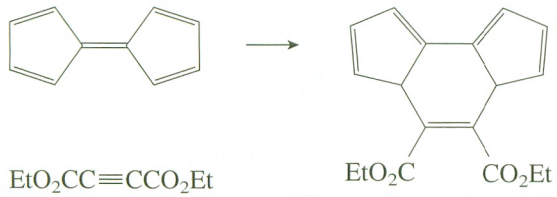
Cycloadditions to form rings larger than six-membered are much less common because of the unfavorable entropy of reactions that form large rings. In simple terms, such reactions are not favorable because collisions with the required geometry—that is, with both ends of the two pi systems colliding simultaneously—are not very probable. However, such reactions are known in cases in which other bonds in the molecule hold the pi system in a reactive geometry. For example, the following cycloaddition has been reported:



This reaction is an [8 + 2] cycloaddition and is thermally allowed. In terms of the pi systems, a 10-membered ring is formed, an entropically unfavorable process. However, the nitrogen holds the ends of the eight-electron pi system close together, so the two-electron component can easily reach them. Counting via the nitrogen, a 5-membered ring is formed, a process that is much more favorable.

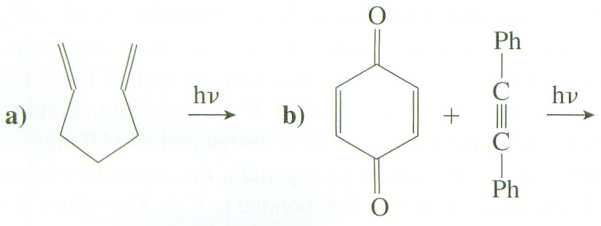
PROBLEMS 22.15

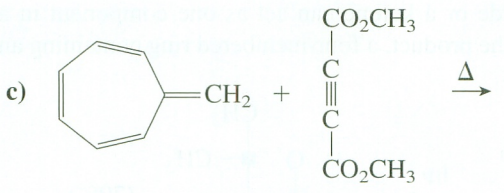
Explain whether you would use heat or light to accomplish this cycloaddition reaction:



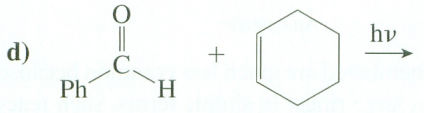
PROBLEMS 22.16

Show the products of these reactions:



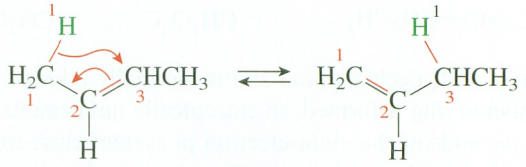


An [8 + 2] cycloaddition



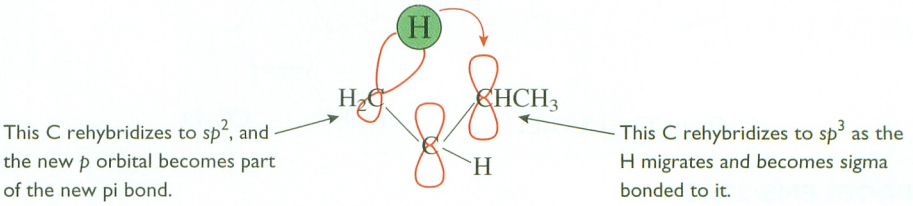
22.8 SIGMATROPIC REARRANGEMENTS

An intramolecular migration of a group along a conjugated pi system is termed a **sigmatropic rearrangement.** Basically, a sigma bond adjacent to a conjugated pi system is broken, the pi bonds are reorganized, and a new sigma bond is formed at the end of the pi system. The reaction shown in the following equation is a simple example of a sigmatropic rearrangement:



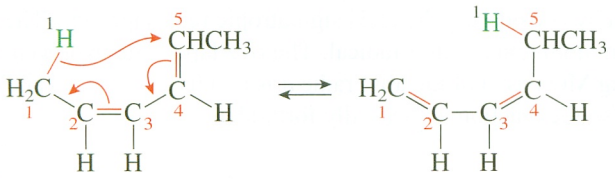
A [1,3] sigmatropic rearrangement

In this reaction a hydrogen that is sigma bonded to the carbon that is adjacent to the pi bond (C-1) migrates to the end carbon of the pi bond (C-3). As this occurs, the pi bond "migrates" from C-2–C-3 to C-1–C-2. A picture of the orbitals involved in this reaction may help make the process clearer:


H
H2C
CHCH3
C
H
This C rehybridizes to sp2, and the new p orbital becomes part of the new pi bond.
This C rehybridizes to sp3 as the H migrates and becomes sigma bonded to it.

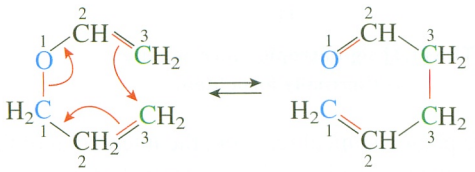
Sigmatropic rearrangements are classified according to the number of bonds separating the migration origin and the migration terminus in each component. To classify the rearrangement, first find the sigma bond that is broken in the reaction. Assign number 1 to *both* of the atoms involved in this bond. Number the atoms of each of the components up to the atoms where the new sigma bond is formed. If the new sigma bond is formed between atoms numbered *i* and *j,* then the reaction is designated an [*i,j*] sigmatropic rearrangement. For example, in the previous rearrangement the sigma bond that is broken connects H-1 to C-1. In the product, H-1 is now bonded to C-3. Therefore, the

reaction is designated a [1,3] sigmatropic rearrangement. The following reaction is similar, except that there is one more pi bond in one component and the hydrogen has migrated to C-5. This reaction is an example of a [1,5] sigmatropic rearrangement.



A [1,5] sigmatropic rearrangement

In addition to rearrangements such as the previous two, it is possible for both of the components to contain pi bonds. In the following reaction the carbon–oxygen bond is broken and the new sigma bond is formed between the carbons at the other end of each of the components. This is an example of a [3,3] sigmatropic rearrangement.

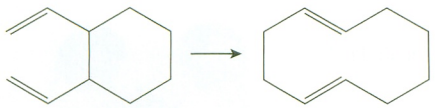


A [3,3] sigmatropic rearrangement

PROBLEM 22.17

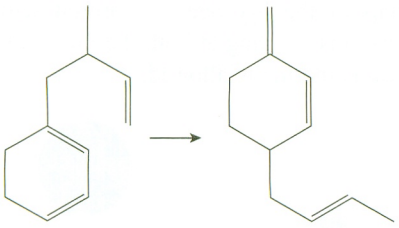
Assign the values for *i* and *j* for these [*i*,*j*] sigmatropic rearrangements:

a)



b) $CH_2CH{=}CHCH{=}CHCH{=}CHCH_3 \longrightarrow CH_2{=}CHCH{=}CHCH{=}CHCHCH_3$ (H on the CH at the right end)

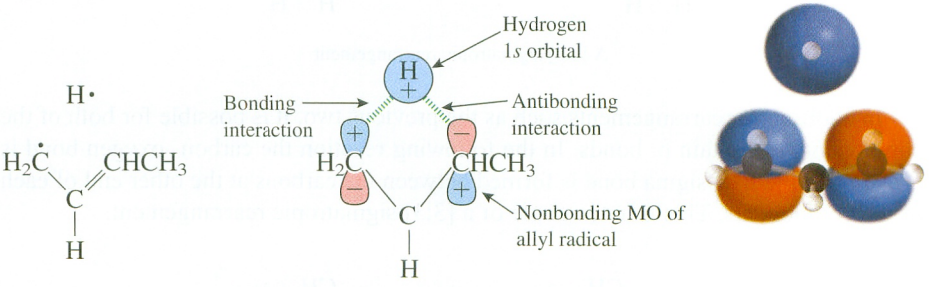
c)



To determine whether a sigmatropic rearrangement is allowed or forbidden, the compound is first imagined to form two radicals by homolytic cleavage of the sigma bond that is broken in the reaction. (Although this analysis pictures the formation of radical intermediates, remember that the reaction is actually concerted.) The interaction of the orbitals of the two radical fragments at the migration origin and the migration terminus are then

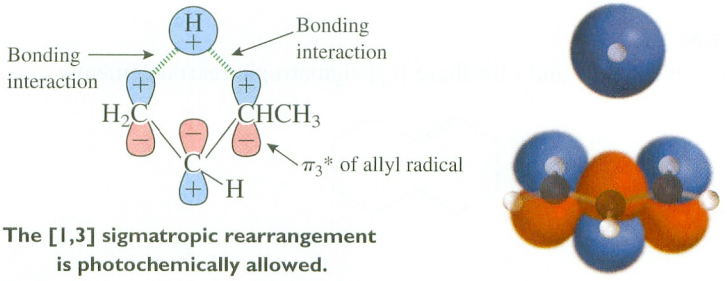
examined. If the overlap of the orbitals of the HOMOs is bonding at both the migration origin and terminus, the reaction is allowed. If one of these overlaps is antibonding, the reaction is forbidden. The radical fragments that are analyzed usually have an odd number of orbitals. In such a case the HOMOs for a thermal reaction are the nonbonding MOs.

Let's begin by considering the [1,3] sigmatropic rearrangement. The two fragments are a hydrogen atom and an allyl radical. The overlap of the hydrogen 1*s* orbital with the nonbonding MO (π_2^{nb}) of the allyl radical is bonding at one end and antibonding at the other end, so the reaction is thermally forbidden.



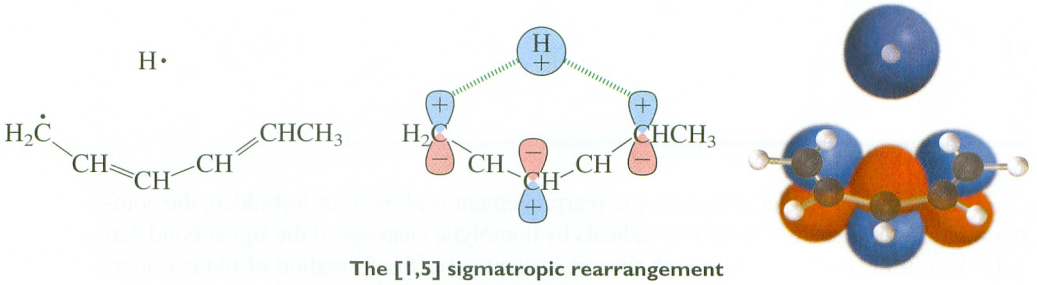
The [1,3] sigmatropic rearrangement is thermally forbidden.

For analysis of the photochemical reaction, the interaction of the hydrogen 1*s* orbital with π_3^* of the allyl system is used. The interaction is bonding at both the migration origin and terminus, so the [1,3] sigmatropic rearrangement is photochemically allowed.



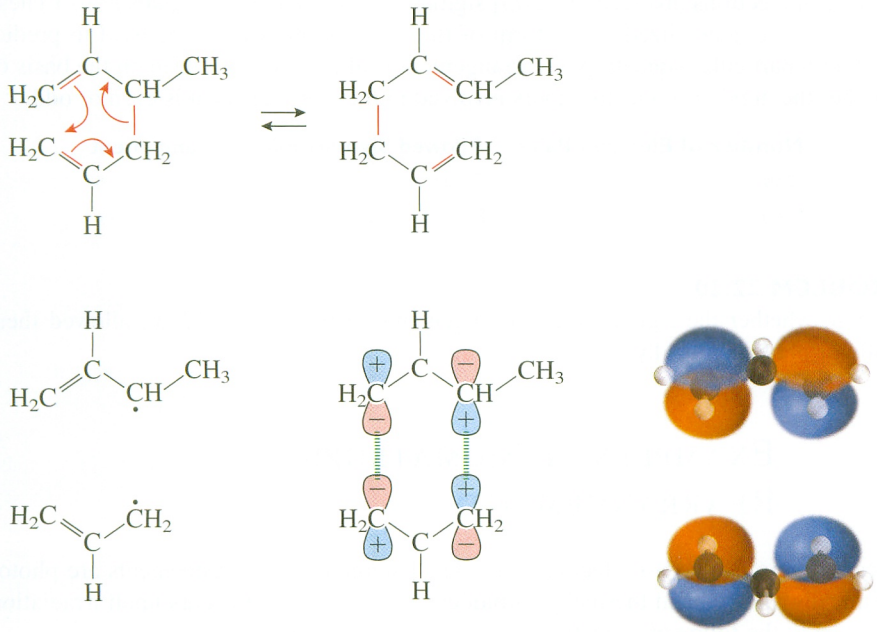
The [1,3] sigmatropic rearrangement is photochemically allowed.

The [1,5] sigmatropic rearrangement is analyzed by examination of a hydrogen atom and a pentadienyl radical. The overlap of the hydrogen 1*s* orbital with the nonbonding MO of the five-orbital system (π_3^{nb}) is bonding at both the migration origin and the migration terminus, so the reaction is thermally allowed.



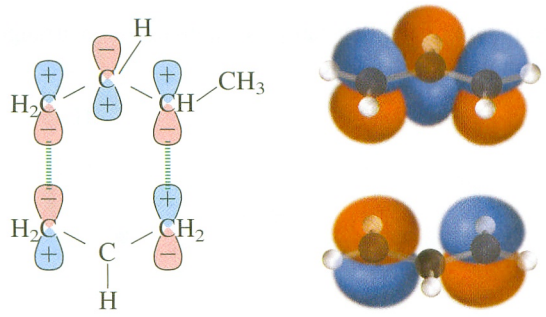
The [1,5] sigmatropic rearrangement is thermally allowed.

A compound rearranging by a [3,3] sigmatropic pathway is split into two allyl radicals. Interaction of the nonbonding MOs of these allyl radicals is bonding at both ends so the reaction is thermally allowed.



The [3,3] sigmatropic rearrangement is thermally allowed.

The interaction of the nonbonding MO of one allyl radical with π_3^* of the other must have one antibonding interaction, so the photochemical [3,3] sigmatropic rearrangement is forbidden.



The [3,3] sigmatropic rearrangement is photochemically forbidden.

PROBLEM 22.18

Use orbital drawings to show that a [1,5] sigmatropic rearrangement is photochemically forbidden.

PROBLEM 22.19

Use orbital drawings to show that a [1,7] sigmatropic rearrangement is thermally forbidden.

The [1,3] sigmatropic rearrangement involves four electrons (two electron pairs) and is photochemically allowed. Both the [1,5] and [3,3] sigmatropic rearrangements involve six electrons (three electron pairs) and are thermally allowed. (Note that the number of electrons involved in an [*i*,*j*] sigmatropic rearrangement equals $i + j$.) These results can be generalized in the form of the chart below that can be used to predict whether a particular sigmatropic rearrangement is allowed or forbidden on the basis of whether the number of electron pairs involved in the rearrangement is even or odd.

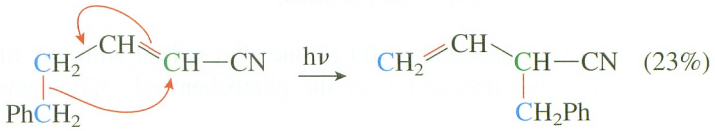
Number of Electron Pairs	Allowed Sigmatropic Rearrangement
Odd	Thermal
Even	Photochemical

PROBLEM 22.20

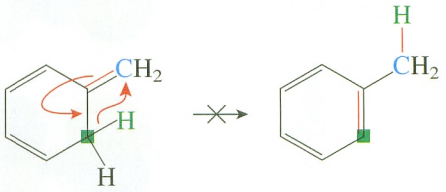
Explain whether the sigmatropic rearrangements of problem 22.17 are allowed thermally or photochemically.

22.9 Examples of Sigmatropic Rearrangements

Because they involve two electron pairs, [1,3] sigmatropic rearrangements are photochemically allowed and thermally forbidden. An example that occurs upon irradiation is shown in the following equation:

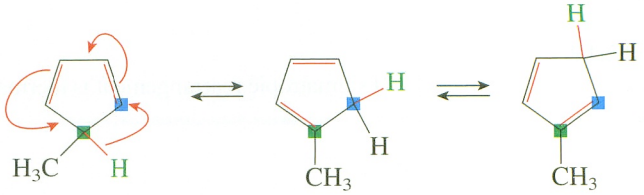


The forbidden nature of the thermal [1,3] sigmatropic rearrangement is illustrated by the following example:



Although the rearrangement of the triene to toluene is highly exothermic, it does not occur at room temperature because the necessary migration is forbidden.

Thermal [1,5] sigmatropic rearrangements are allowed and are quite common. This process is responsible for the interconversion of the methylcyclopentadiene isomers, which proceeds with a half-life of about 1 h at 20°C.



[3,3] Sigmatropic rearrangements are also thermally allowed and are quite important in synthesis. When the six atoms involved are all carbons, the reaction is known as the **Cope rearrangement.** An example is shown in the following equation:

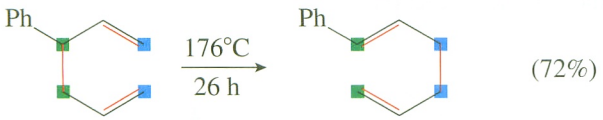
15% 85%

As is the case with all of these reactions, the process is allowed in both directions, so a mixture of the reactant and product results if the equilibrium constant does not dramatically favor one over the other. Many Cope rearrangements produce such a mixture because the reactant and the product are comparable in stability.

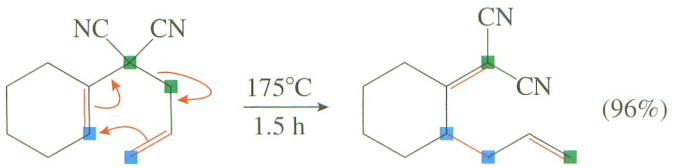
However, factors such as ring strain or conjugation can make one product predominate at equilibrium. For example, the cyclopropane derivative shown in the following equation is stable at −20°C but rearranges completely to 1,4-cycloheptadiene at room temperature. The equilibrium is driven toward the product by relief of ring strain.

1,4-Cycloheptadiene

The following two equations provide examples in which the product of the Cope rearrangement is favored because it is stabilized by conjugation:

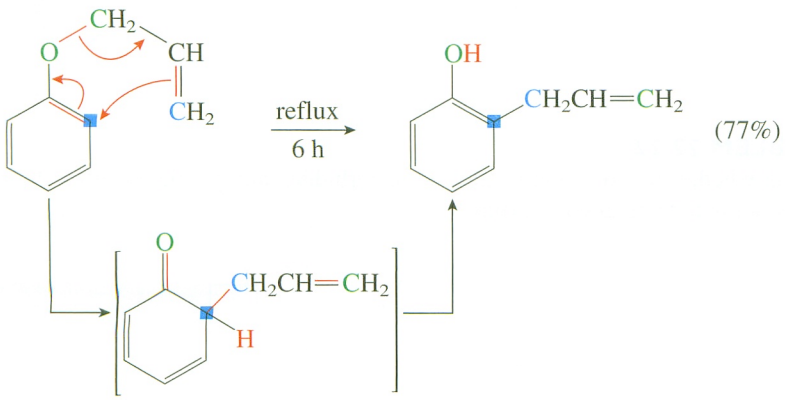


(72%)



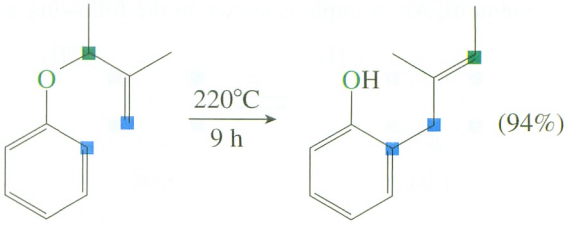
(96%)

The oxygen analog of the Cope rearrangement is called the **Claisen rearrangement.** Often, one of the pi bonds is part of an aromatic ring, as shown in the following example:



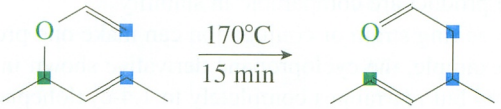
(77%)

In these cases the initially formed product spontaneously tautomerizes to regain its aromatic stabilization. Another example is provided in the following equation:

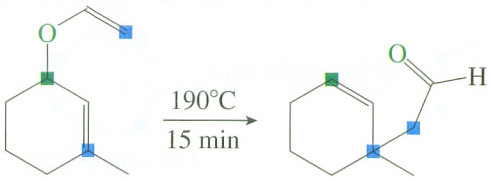


(94%)

Claisen rearrangements also occur with nonaromatic substrates. In these reactions the formation of the strong carbon–oxygen double bond drives the equilibrium to completion:



(90%)



(93%)

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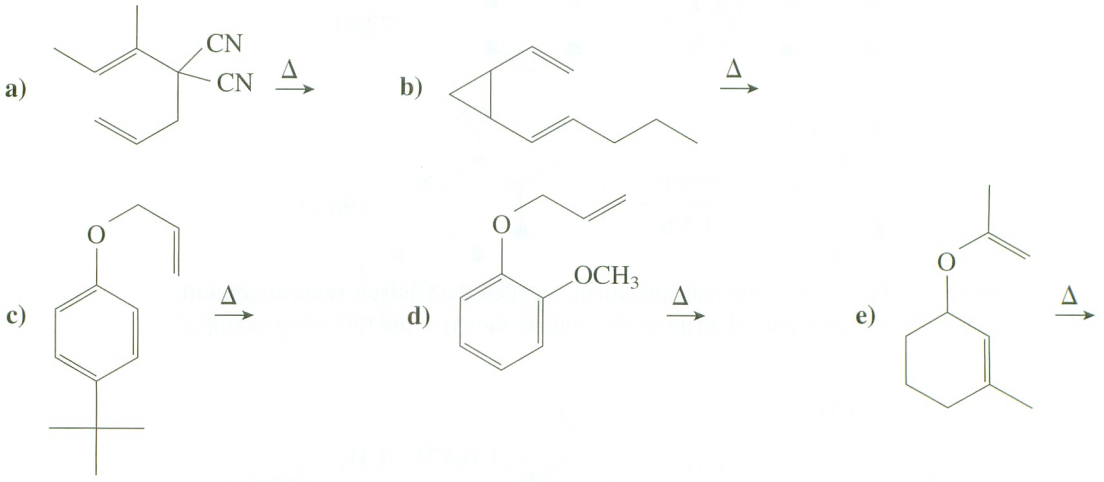
Click *Coached Tutorial Problems* for more practice with **Sigmatropic Rearrangements.**

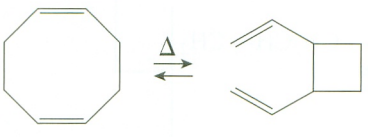
PROBLEM 22.21

Show the products of these reactions:



PROBLEM 22.22

Explain whether this reaction is allowed or forbidden and predict whether the reactant or product is favored at equilibrium.



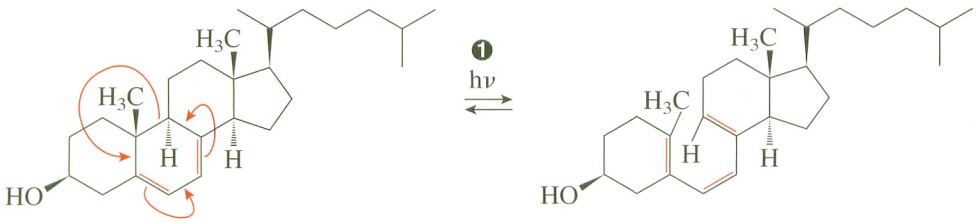
Focus On Biological Chemistry

Pericyclic Reactions and Vitamin D

Vitamin D is necessary for the proper deposition of calcium in growing bones. A deficiency of this vitamin leads to the disease known as rickets. You may have heard that sunlight contains vitamin D. Of course, there are no chemical compounds, or vitamins, in sunlight, but animals require sunlight to make vitamin D.

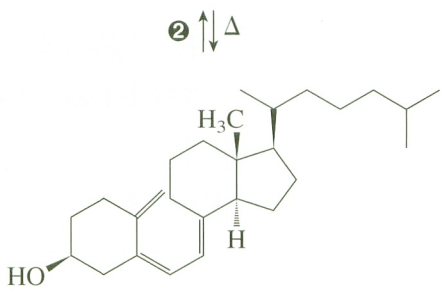
In the skin of animals, 7-dehydrocholesterol is converted to vitamin D_3 by the reaction sequence that follows. The first step in this process, the conversion of 7-dehydrocholesterol to pre-cholecalciferol, requires light. This is an electrocyclic reaction and must occur by a conrotatory motion to avoid the formation of a highly strained trans double bond in one of the rings. Conrotation involving three pairs of electrons must occur photochemically to be allowed.

❶ In the skin of animals, 7-dehydrocholesterol is converted to pre-cholecalciferol by the action of sunlight. This electrocyclic reaction must occur in a conrotatory fashion to avoid forming a trans double bond in one of the rings. Because three electron pairs are involved, this reaction is photochemically allowed.



7-Dehydrocholesterol — Pre-cholecalciferol

❷ The second step is a [1,7] sigmatropic rearrangement and has been shown to occur thermally. Because it involves four electron pairs, to be thermally allowed it must occur with an unusual geometry, where the hydrogen migrates from the top of the pi system on one end to the bottom of the pi system on the other.

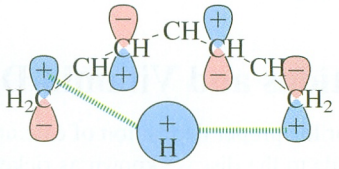


Cholecalciferol (vitamin D_3)

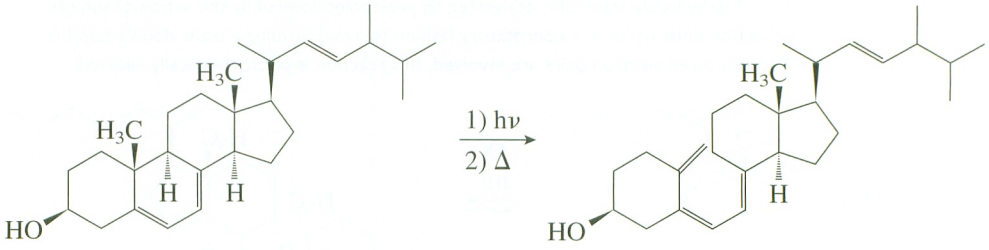
The second step of this process, the conversion of pre-cholecalciferol to cholecalciferol or vitamin D_3, is also a pericyclic reaction. It is a [1,7] sigmatropic rearrangement that has been demonstrated to occur thermally. To be thermally allowed, a sigmatropic rearrangement involving four pairs of electrons must occur with an unusual geometry where the hydrogen migrates from the top of the pi system on one end

Continued

to the bottom of the pi system on the other, as shown in the following diagram. The required geometry is readily attainable for pre-cholecalciferol.



H. Steenbock, at the Wisconsin Agricultural Research Station, discovered that irradiation of rat food was able to cure rickets in rats. He patented the process of using ultraviolet irradiation to enrich the compound that helps prevent rickets in a variety of foods. (During 1925–1945, this patent generated about 14 million dollars, which was used to support research in Wisconsin.) Eventually, it was determined that the vitamin (vitamin D_2) that is present in these foods was produced from ergosterol, a steroid that is very similar to 7-dehydrocholesterol, differing only in the structure of its side chain. On irradiation, ergosterol is converted to calciferol or vitamin D_2 by the same mechanism as 7-dehydrocholesterol. This is the "vitamin D" that is added to milk.

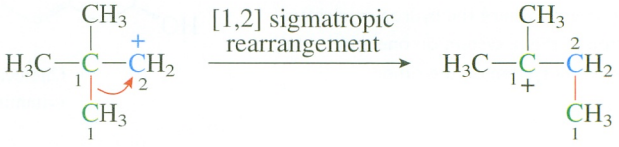


Ergosterol

Calciferol
(vitamin D_2)

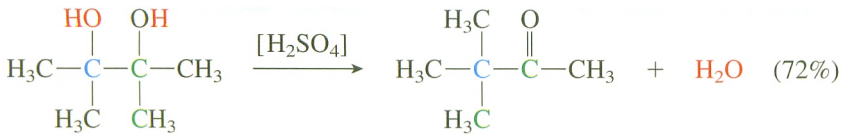
22.10 Rearrangements to Electron-Deficient Centers

The rearrangements of carbocations that were first encountered in Chapter 8 can be classified as [1,2] sigmatropic rearrangements:



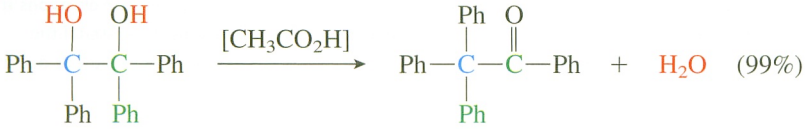
These rearrangements involve one pair of electrons; therefore, they are thermally allowed. We have already seen that they are very common. In contrast, the corresponding rearrangement of carbanions involves two electron pairs and is thermally forbidden. This is why carbanion rearrangements are rare.

The **pinacol rearrangement** is a useful reaction that proceeds via a carbocation rearrangement. Treatment of 2,3-dimethyl-2,3-butanediol, also known as pinacol, with acid results in the formation of a ketone, pinacolone:



Pinacol Pinacolone

The mechanism for this reaction, shown in Figure 22.5, involves a carbocation rearrangement that occurs by an allowed [1,2] sigmatropic shift. The product of this rearrangement, a protonated ketone, is considerably more stable than the initial carbocation, so the migration is quite favorable. Another example of the pinacol rearrangement is provided in the following equation:

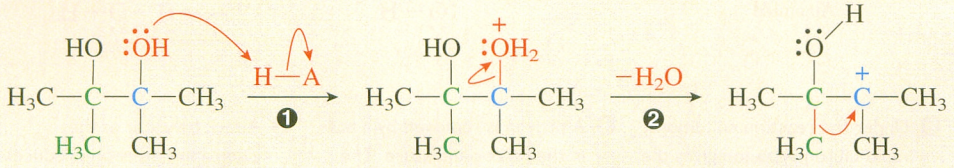


The mechanism for the pinacol rearrangement contains no surprises. It consists only of steps that have been encountered previously.

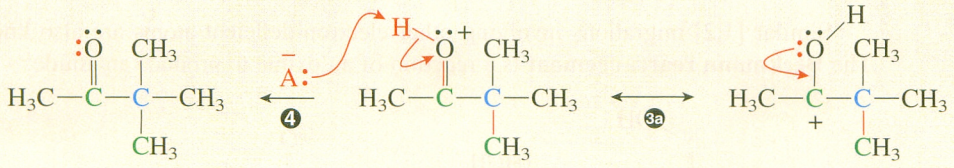
❶ Oxygen is protonated by the acid.

❷ Water leaves to generate a carbocation.

❸ Although this carbocation is tertiary, it rearranges to a cation that is even more stable by migration of a methyl group by an allowed [1,2] sigmatropic rearrangement.



Pinacol



Pinacolone

❹ Loss of a proton gives the final product, a ketone.

3a This cation is a protonated ketone and is considerably more stable than the initial carbocation because the octet rule is satisfied at all of the atoms.

Figure 22.5

MECHANISM OF THE PINACOL REARRANGEMENT.

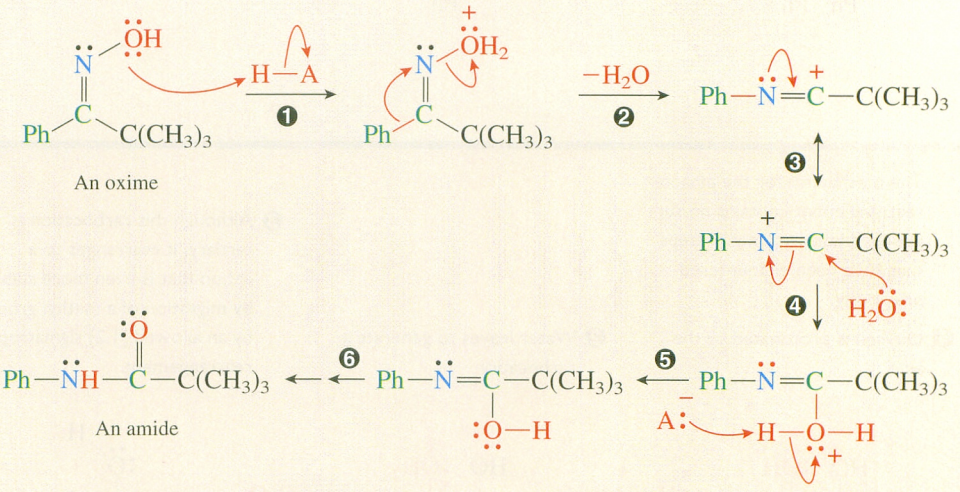
Figure 22.6

MECHANISM OF THE BECKMANN REARRANGEMENT.

❶ The reaction begins by protonation of the oxygen of the oxime.

❷ As water leaves, positive charge builds up on the nitrogen. If this continues, a nitrogen with six electrons and a positive charge—the nitrogen analog of a carbocation—would be generated. Because nitrogen is more electronegative than carbon, such a species is much less stable than a carbocation. To avoid forming this highly energetic ion, the phenyl group migrates to the nitrogen as the water leaves.

❸ The product of the rearrangement has the positive charge on the carbon and is stabilized by resonance delocalization of the positive charge onto the nitrogen. The lower resonance structure is the major contributor to the resonance hybrid because it has the octet rule satisfied at both the carbon and the nitrogen. It is quite different from the positive nitrogen with six electrons that would be generated if the rearrangement did not occur.

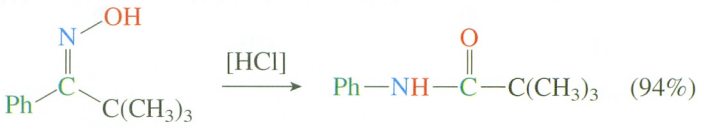


❻ Under the reaction conditions, rapid tautomerization gives the final product, an amide (see Chapter 19).

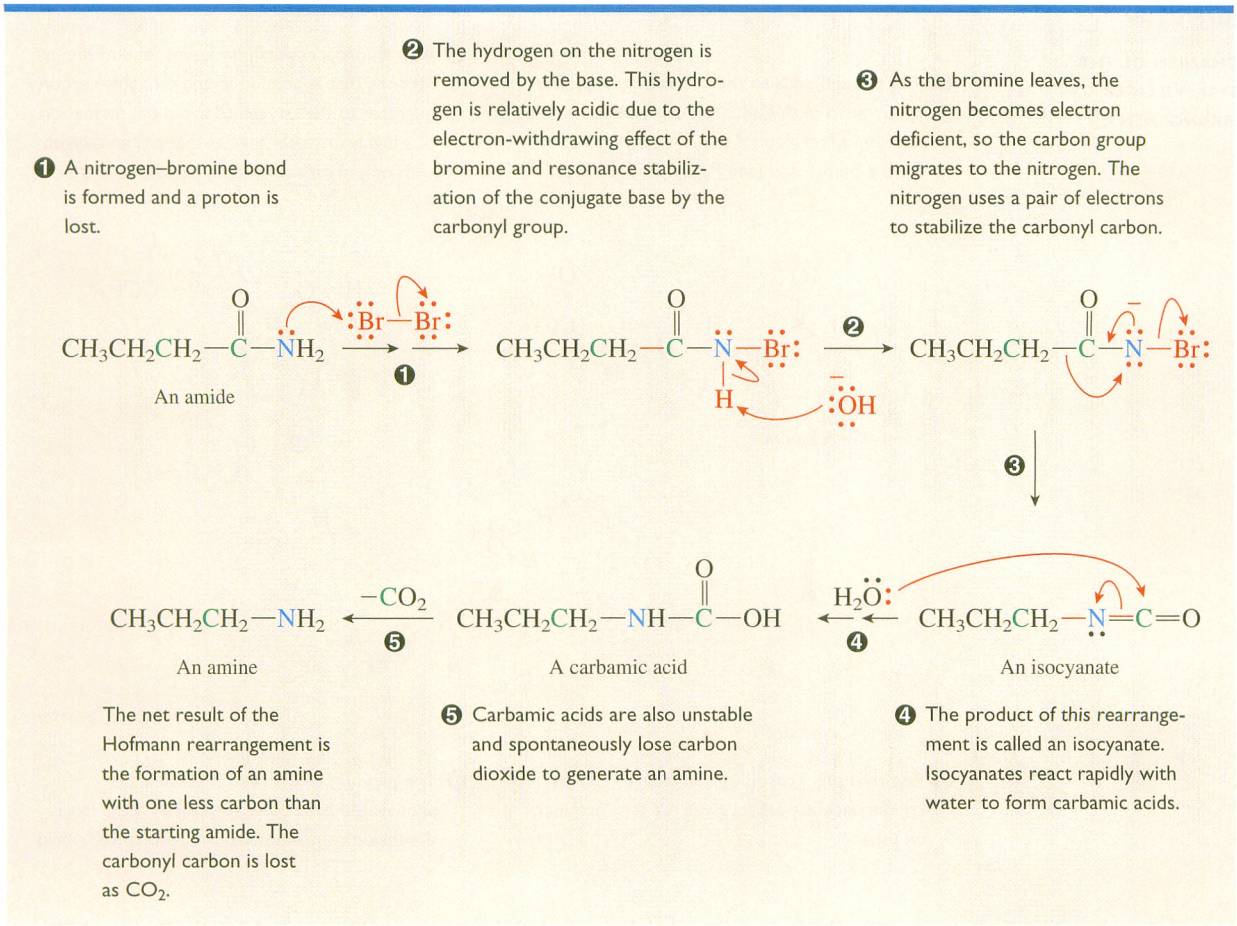
❺ A proton is removed by a base in the reaction mixture. The compound that results is a tautomer of an amide.

❹ Attack by water at the electrophilic carbon produces this ion.

Similar [1,2] migrations involving other electron-deficient atoms are also known. The **Beckmann rearrangement** is a reaction of an oxime to produce an amide:



The mechanism for this reaction, shown in Figure 22.6, proceeds via an allowed [1,2] sigmatropic rearrangement to an electron-deficient nitrogen. Another example of the Beckmann rearrangement is provided in the following equation:


❶ A nitrogen–bromine bond is formed and a proton is lost.
❷ The hydrogen on the nitrogen is removed by the base. This hydrogen is relatively acidic due to the electron-withdrawing effect of the bromine and resonance stabilization of the conjugate base by the carbonyl group.
❸ As the bromine leaves, the nitrogen becomes electron deficient, so the carbon group migrates to the nitrogen. The nitrogen uses a pair of electrons to stabilize the carbonyl carbon.
An amide
An amine
A carbamic acid
An isocyanate
The net result of the Hofmann rearrangement is the formation of an amine with one less carbon than the starting amide. The carbonyl carbon is lost as CO_2.
❺ Carbamic acids are also unstable and spontaneously lose carbon dioxide to generate an amine.
❹ The product of this rearrangement is called an isocyanate. Isocyanates react rapidly with water to form carbamic acids.

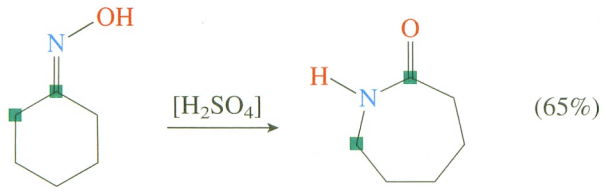
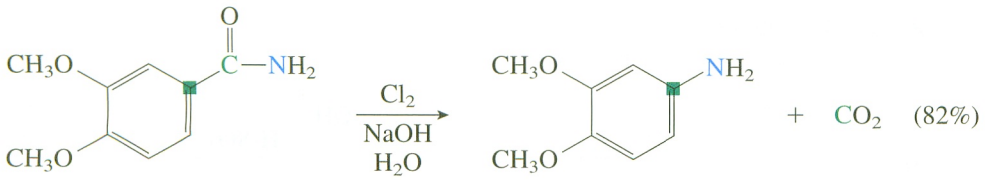


Figure 22.7
MECHANISM OF THE HOFMANN REARRANGEMENT.

The **Hofmann rearrangement** also involves a migration to an electron-deficient nitrogen. In this case, an amide is treated with Cl_2 or Br_2 in aqueous base, resulting in the formation of an amine with one less carbon. The original carbonyl carbon is lost as carbon dioxide. The mechanism is shown in Figure 22.7 and an example is provided by the following equation:



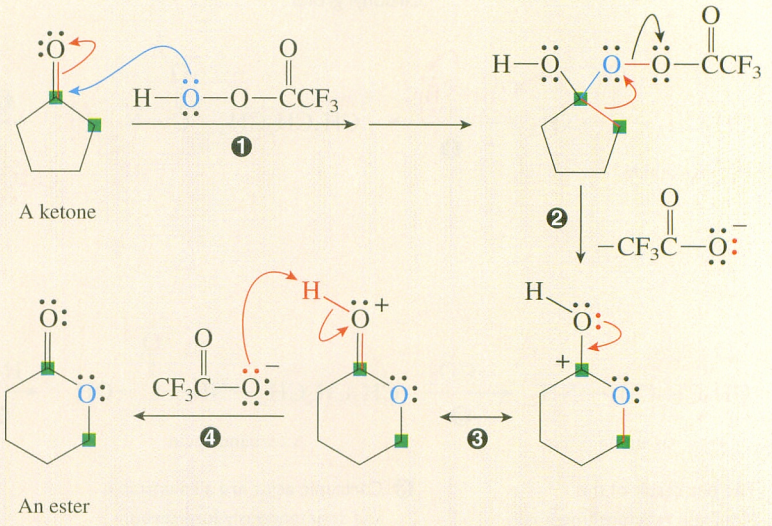
An amide — An amine with one less carbon

Figure 22.8

MECHANISM OF THE BAEYER-VILLIGER REARRANGEMENT.

❶ The peracid adds to the carbonyl group. The mechanism of this addition is analogous to the addition of an alcohol to a carbonyl group to form a hemiacetal (see Figure 18.5, p. 776).

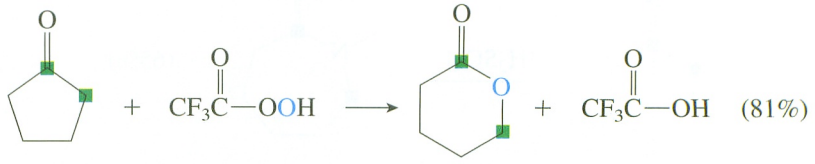
❷ As trifluoroacetate anion leaves, one of the carbons that is bonded to the carbonyl carbon migrates to the oxygen to avoid the formation of a highly unstable species that has an oxygen with only six electrons and a positive charge.



❹ Removal of a proton by some base, such as trifluoroacetate anion, gives the final product, an ester.

❸ The product of the rearrangement is a protonated ester. The structure on the left is the major contributor to the resonance hybrid.

Similar migrations to electron-deficient oxygen also occur. In the **Baeyer-Villiger rearrangement** a ketone is reacted with a peracid. The product is an ester in which one of the alkyl groups of the ketone has migrated to oxygen:

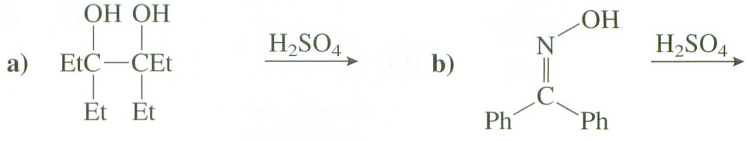


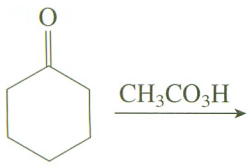
A ketone A peracid An ester

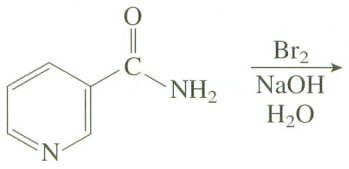
The mechanism for this reaction, outlined in Figure 22.8, is similar to that for the Beckmann rearrangement. As a group leaves from the oxygen, a carbon group migrates to this electron-deficient oxygen by an allowed [1,2] sigmatropic rearrangement.

PROBLEM 22.23

Show the products of these reactions:

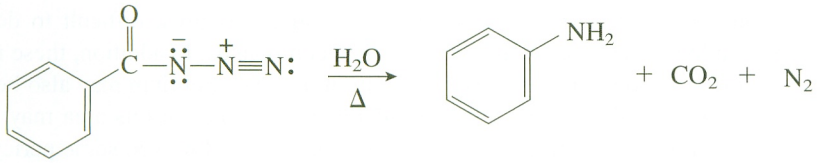


c) 

d) 

PROBLEM 22.24

The following reaction is known as the Curtius rearrangement. Its mechanism is similar to the Hofmann rearrangement. Show the mechanism of this reaction.



Review of Mastery Goals

After completing this chapter, you should be able to:

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- Show the energies and nodal properties of the pi MOs of a small conjugated system, whether it is composed of an even or odd number of orbitals. (Problem 22.25)
- Classify reactions as electrocyclic reactions, [$x + y$] cycloadditions, or [i,j] sigmatropic rearrangements. (Problem 22.30)
- Use the pi MOs to explain whether these reactions are allowed or forbidden. (Problem 22.29)
- Show the products, including stereochemistry, of any of these reactions. (Problems 22.26 and 22.27)
- Show the mechanisms of the pinacol, Beckmann, Hofmann, and Baeyer-Villiger rearrangements. (Problems 22.36, 22.37, 22.38, and 22.39)
- Use the principles of pericyclic reactions to explain the mechanism, selectivity, and stereochemistry of a concerted reaction. (Problems 22.35, 22.40, 22.41, 22.42, 22.43, 22.44, 22.45, 22.46, 22.47, 22.48, and 22.49)
- Use the reactions in syntheses. (Problems 22.28, 22.31, 22.32, and 22.34)

Visual Summary of Key Reactions

The concerted reactions presented in this chapter are called pericyclic reactions. They are divided into electrocyclic reactions, cycloaddition reactions, and sigmatropic rearrangements. Some occur when energy is supplied in the form of heat; others require light energy to occur. Most have strict stereochemical requirements.

Whether a particular pericyclic reaction is allowed or not can be determined by examination of the interaction of the molecular orbitals where the new bonds are forming.

The rules for disrotatory electrocyclic reactions, cycloadditions, and sigmatropic rearrangements are summarized in the accompanying chart:

Number of Electron Pairs	Allowed Reaction
Odd	Thermal
Even	Photochemical

The selection rules for conrotatory electrocyclic reactions are the opposite of those just listed; that is, for a molecule with an even number of electron pairs, conrotation is thermally allowed, and for a molecule with an odd number of electron pairs, conrotation is photochemically allowed.

For many compounds there are several possible allowed pericyclic reactions. On the basis of your limited experience in organic chemistry, it is often difficult to decide which of the allowed reactions will occur for such compounds. In addition, these reactions are allowed in both directions, so the position of the equilibrium may also be important. Even an organic chemist with considerable experience in this area may have difficulty predicting exactly what will happen in every case. However, some pericyclic reactions are more common than others. Table 22.1 summarizes those that are encountered most often.

Table 22.1 Summary of Pericyclic Reactions

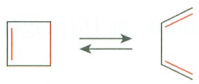
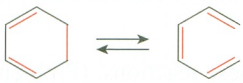
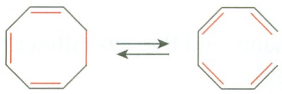
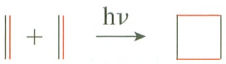
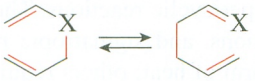
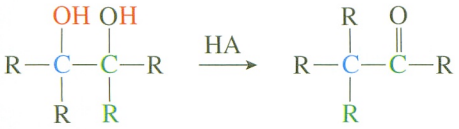
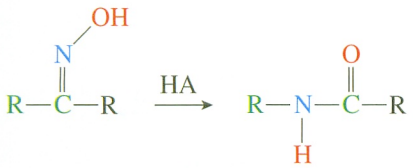
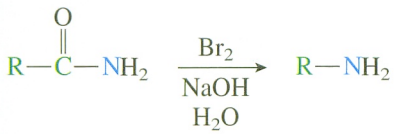
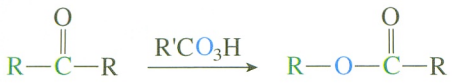
Reaction	Comments
Electrocyclic Reactions (Section 22.4)	
	Thermal: conrotation Photochemical: disrotation
	Thermal: disrotation Photochemical: conrotation
	Thermal: conrotation Photochemical: disrotation
Cycloaddition Reactions (Sections 22.7 and 22.6)	
	[2 + 2] Cycloaddition, photochemically allowed
	[4 + 2] Cycloaddition, Diels-Alder reaction, thermally allowed
Sigmatropic Rearrangements (Section 22.9)	
	[3,3] Sigmatropic rearrangement, thermally allowed, when X = C, Cope rearrangement, when X = O, Claisen rearrangement

Table 22.1 Summary of Pericyclic Reactions—cont'd

Reaction	Comments
Electron-Deficient Rearrangements (Section 22.10)	
	Pinacol rearrangement
	Beckmann rearrangement
	Hofmann rearrangement
	Baeyer-Villiger rearrangement

Additional Problems

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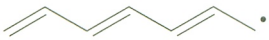
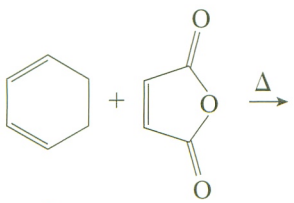
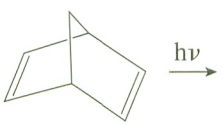
22.25 Show the energies for the pi MOs of these species. Show the electrons occupying the MOs for each.

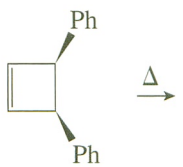
a) Lowest-energy excited state of

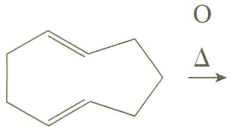
b) Ground state of 

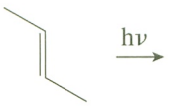
22.26 Show the products of these reactions:

a) 

b) 

c) 

d) 

e) 

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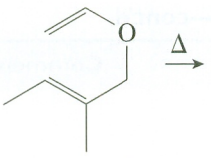
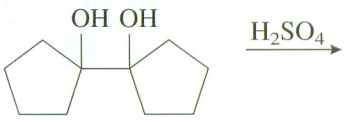
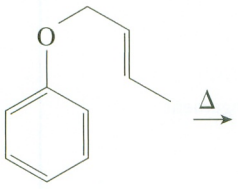
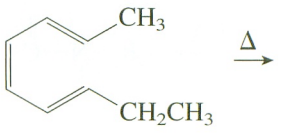
g) 

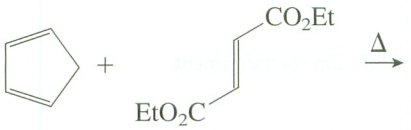
h) 

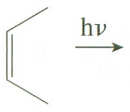
i)

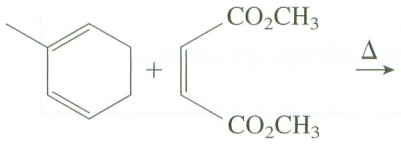
22.27 Show the products of these reactions:

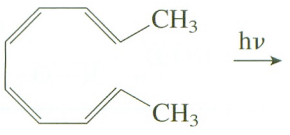
a) 

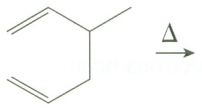
b) 

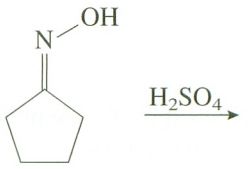
c) 

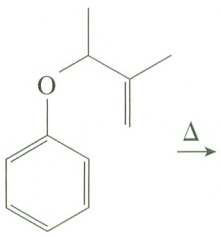
d) 

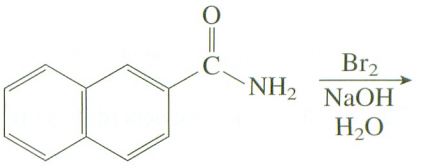
e) 

f) 

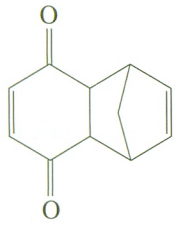
g) 

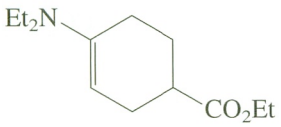
h) 

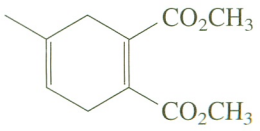
i) 

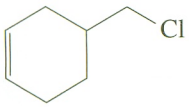
j) 

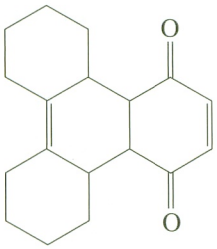
22.28 Show the dienes and dienophiles that could be used to prepare these compounds by Diels-Alder reactions:

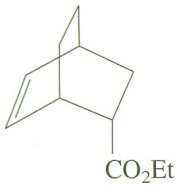
a) 

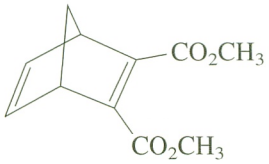
b) 

c) 

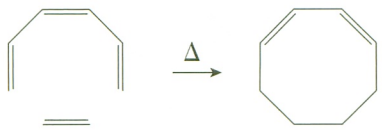
d) 

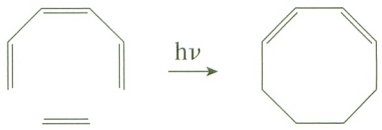
e) 

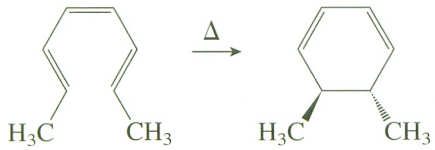
f) 

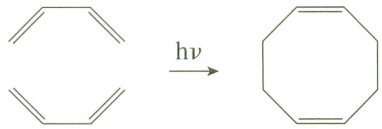
g) 

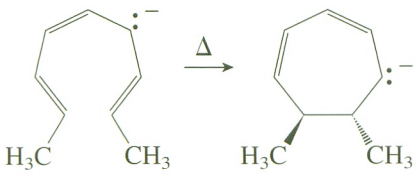
22.29 Use orbital drawings to determine whether these reactions are allowed or forbidden:

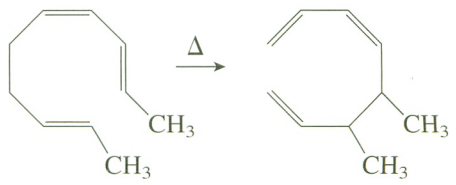
a) 

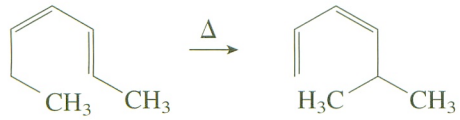
b) 

c) 

d) 

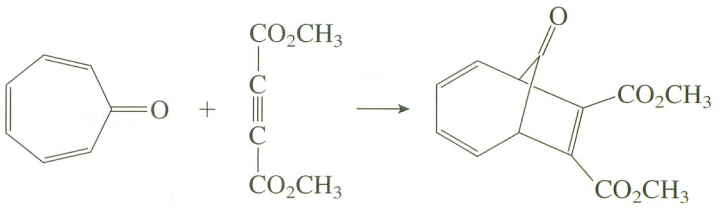
e) 

f) 

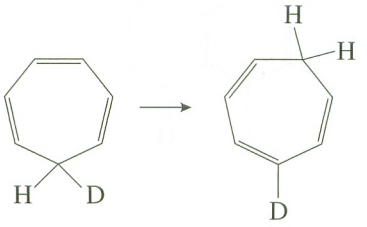
g) 

22.30 Classify these reactions as electrocyclic reactions, [$x + y$] cycloadditions, or [i,j] sigmatropic rearrangements and explain whether each is allowed thermally or photochemically.

a)



b)



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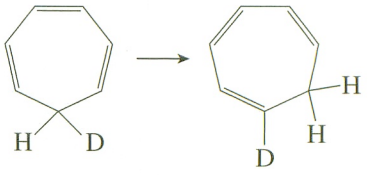

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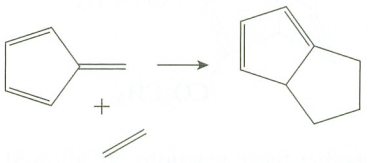

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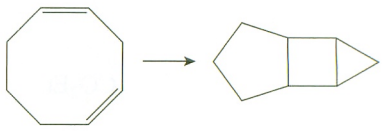

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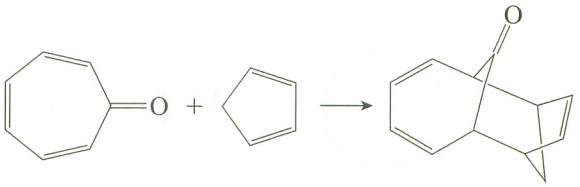

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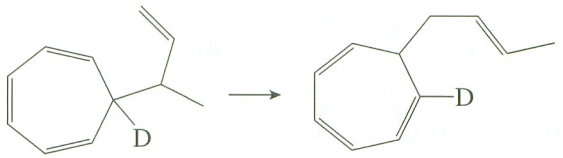

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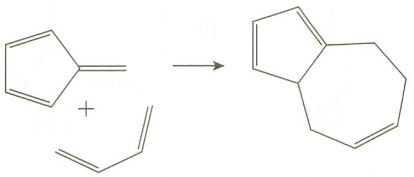
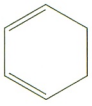
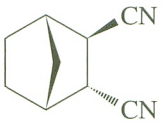
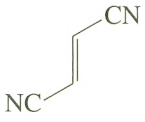
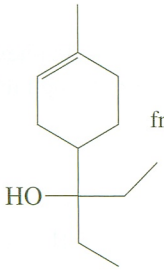
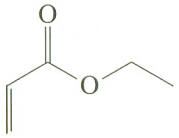
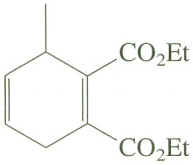


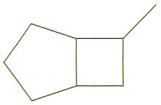
22.31 Show syntheses of these compounds from the indicated starting materials. Reactions from previous chapters may be needed in some cases.

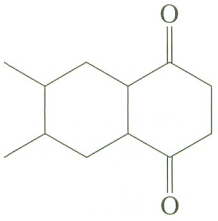
a) from 

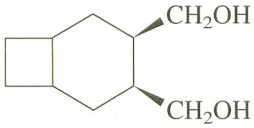
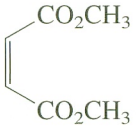
b)  from 

c)  from 

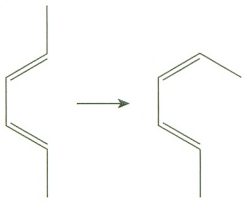
d)  from compounds without rings

e)  from

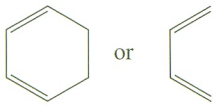
f)  from a compound with one ring

g)  from  and compounds without rings

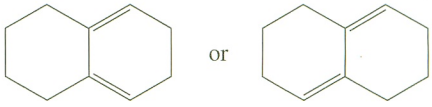
22.32 Suggest a method to convert (2*E*,4*E*)-hexadiene to (2*E*,4*Z*)-hexadiene in a manner so that the stereochemistry is controlled at each step of the process:



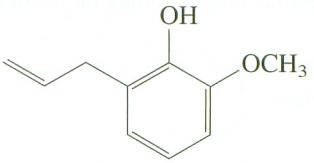
22.33 Explain which compound is more reactive as a diene in the Diels-Alder reaction:

a) 

b)

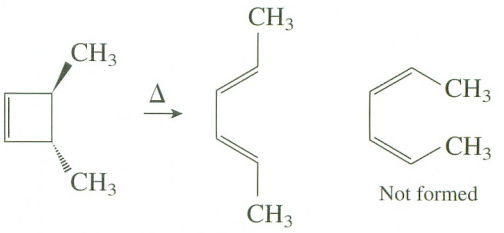
c) 

22.34 Suggest a method for the synthesis of *o*-eugenol from *o*-methoxyphenol:



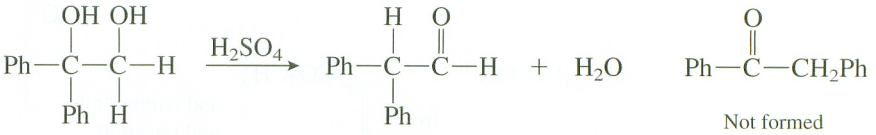
o-Eugenol

22.35 Explain why *trans*-3,4-dimethylcyclobutene produces (2*E*,4*E*)-hexadiene upon heating, whereas (2*Z*,4*Z*)-hexadiene is not formed, even though its formation is an allowed reaction.



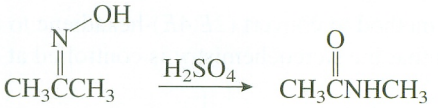
Not formed

22.36 Show all of the steps in the mechanism for this reaction and explain why the aldehyde is formed rather than the ketone:

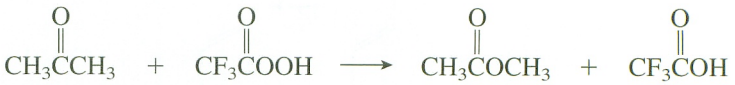


Not formed

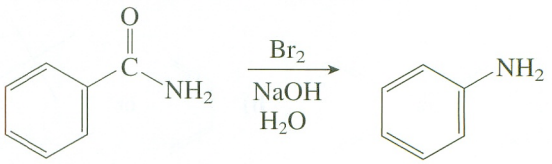
22.37 Show all of the steps in the mechanism for this reaction:



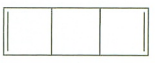
22.38 Show all of the steps in the mechanism for this reaction:



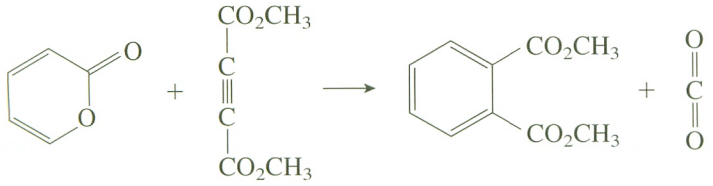
22.39 Show all of the steps in the mechanism for this reaction:



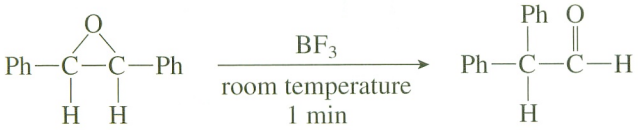
22.40 Attempts to prepare cyclobutadiene usually result in the isolation of this compound. Explain how the formation of this dimer from cyclobutadiene is allowed.



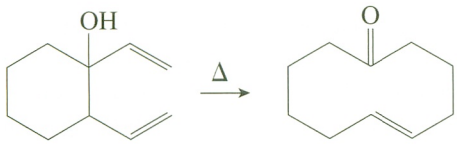
22.41 This reaction has been shown to occur in two thermally allowed steps. Show the structure of the intermediate in the reaction and explain why each step is allowed.



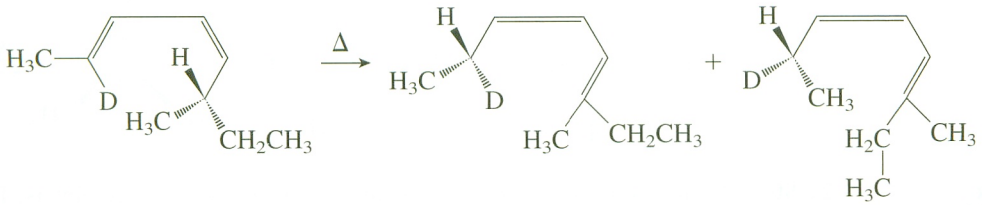
22.42 Suggest a mechanism for this reaction:



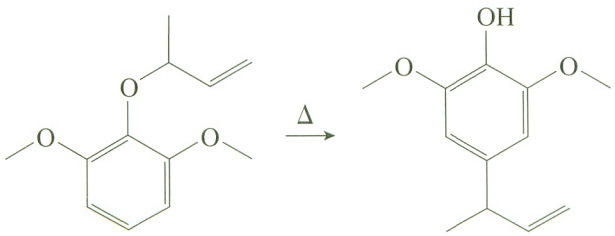
22.43 Suggest a mechanism for this reaction:



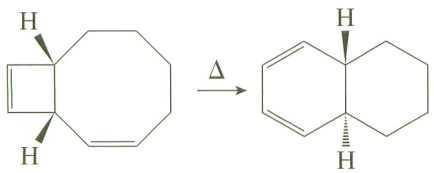
22.44 Explain the stereochemistry of this reaction:



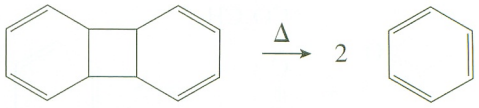
22.45 This reaction has been shown to occur in two thermally allowed steps. Show the structure of the intermediate in the reaction and explain why each step is allowed.



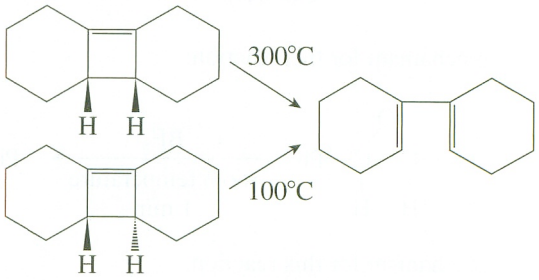
22.46 Suggest a mechanism for this reaction:



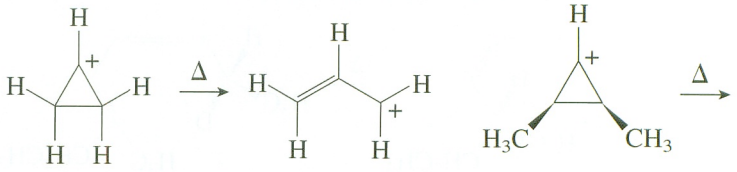
22.47 Explain why this reaction is highly exothermic. Then offer a reason why the reactant is quite stable at room temperature.



22.48 Explain the large difference in the temperatures required for these reactions.

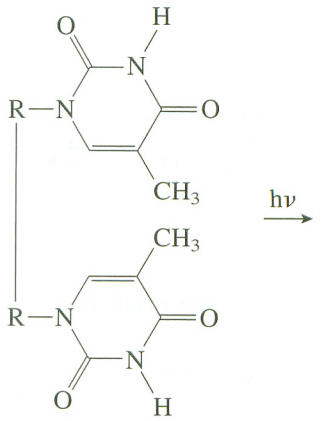


22.49 Cyclopropyl carbocations react rapidly to form allyl carbocations. Explain how this process is allowed. Explain why the allyl carbocation is more stable than the cyclopropyl carbocation. Predict the stereochemistry of the allyl carbocation that is formed from the following *cis*-dimethylcyclopropyl carbocation:

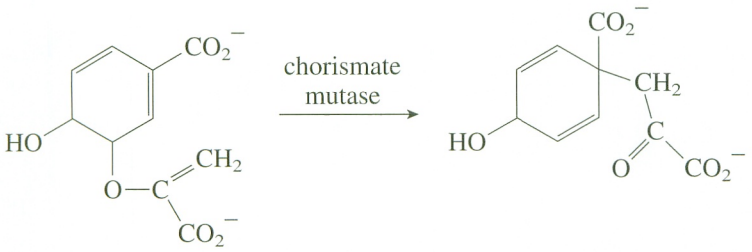


BioLink

22.50 UV radiation causes adjacent thymine bases of DNA to form dimers. The resulting dimers inhibit the normal functioning of DNA and may lead to cancer. Suggest a structure for the thymine dimer that is formed in the following reaction:



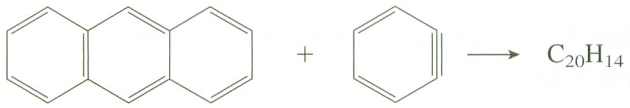
22.51 The conversion of chorismate to prephenate, catalyzed by the enzyme chorismate mutase, is involved in the biosynthesis of the amino acids phenylalanine and tyrosine. Classify this pericyclic reaction and explain whether it is thermally allowed or not.



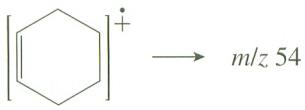
Chorismate Prephenate

Problems Involving Spectroscopy

22.52 The reaction of anthracene with benzyne gives a product, $C_{20}H_{14}$, that shows only four peaks in its ^{13}C-NMR spectrum. Show the structure of this product and explain its formation.

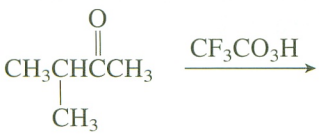


22.53 The mass spectrum of cyclohexene shows a peak at *m/z* 54. Show a structure for this fragment and suggest a mechanism for its formation.

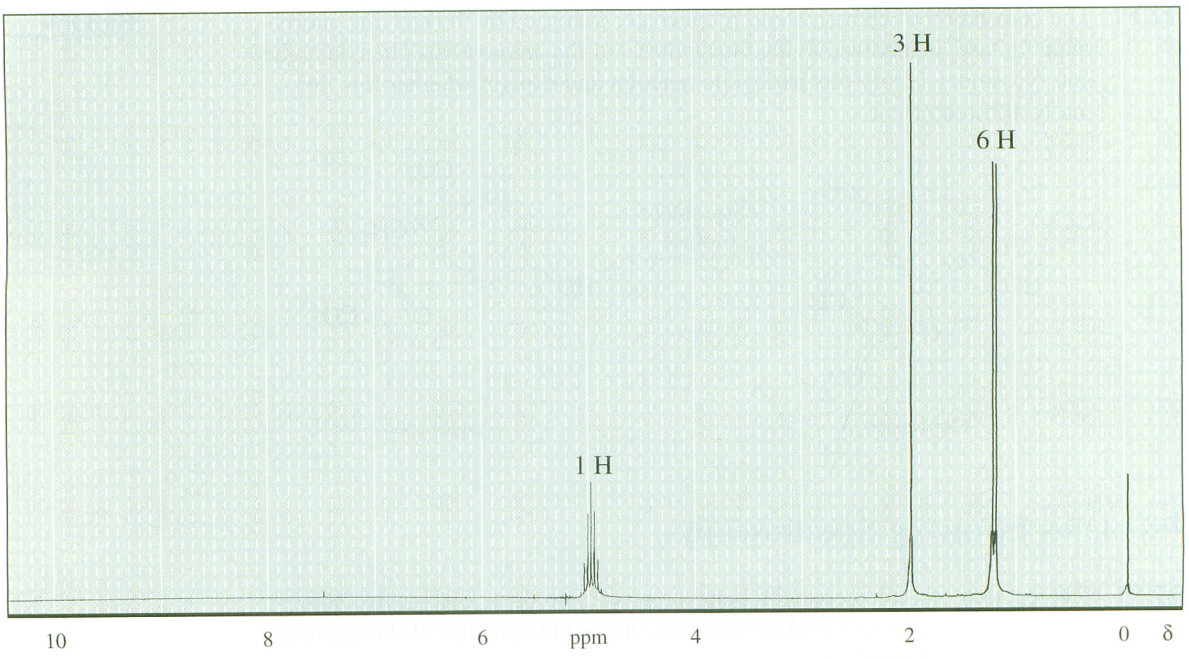


m/z 82

22.54 With unsymmetrical ketones the Baeyer-Villiger reaction can, in principle, give two products. Usually, one product dominates. The ^1H-NMR spectrum of the product isolated from the Baeyer-Villiger reaction of 3-methyl-2-butanone is shown here. Show the structure of this product.



3-Methyl-2-butanone



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Problems Using Online Three-Dimensional Molecular Models

22.55 Explain whether each of these electrocyclic reactions proceeds by conrotation or disrotation.

22.56 Explain whether each of these electrocyclic reactions is thermally allowed or photochemically allowed.

22.57 Explain which product is formed upon heating the octatriene reactant shown. Explain which product is formed when the octatriene is irradiated with ultraviolet light.

22.58 Show the diene and dienophile that would form this cyclohexene derivative in a Diels-Alder reaction.

22.59 Explain which diene shown is more reactive in the Diels-Alder reaction.

22.60 Explain which product is formed from the Diels-Alder reaction of cyclopentadiene with maleic anhydride.

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